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(54) Title: CRYSTALLINE FRAP COMPLEX

(57) Abstract

The invention relates to the human protein FRAP, and in particular to the FKBP12-rapamycin binding domain thereof and to the ternary complex formed by the FRB domain, rapamycin and FKBP12. A new crystalline composition comprising the ternary complex, coordinates defining its three dimensional structure in atomic detail, and uses thereof are disclosed.

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Crystalline FRAP C mplex

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Field of the Invention

The invention relates to a complex, in crystalline form, of two proteins, FKBP12 and the FRB domain of FRAP, in association with rapamycin, a small organic molecule to which the proteins bind. The crystalline form of this ternary complex is particularly useful for the determination of the three-dimensional structure of the complex at the atomic level. The three dimensional structure provides information useful for the design of pharmaceutical compositions which inhibit the biological function of proteins such as FRAP which contain an FRB domain, particularly those biological functions mediated by molecular interactions involving rapamycin or other compounds capable of binding to an FRB domain.

Background

Rapamycin (sometimes called sirolimus) was first described in 1975 as an antifungal agent isolated from Streptomyces hygroscopicus (Vezina, 1975; Sehgal, 1975). In 1987, the structurally related compound FK506 (sometimes called tacrolimus) was characterized as a potent immunosuppressive agent (Tanaka, 1987), and shortly thereafter, rapamycin was also shown to have potent immunosuppressive activity. In spite of rapamycin's immunosuppressive activity and structural similarity to FK506, the two compounds suppress the immune response in completely different ways (Schreiber, 1992). FK506 inhibits the T cell receptor (TCR) signal and prevents activation of a resting helper T cell. Rapamycin inhibits the autocrine signaling pathway involving interleukin-2 (IL-2) and the IL-2 receptor (IL-2R). These latter signals commit the cell to a program of cell division by communicating with the components of the cell cycle machinery necessary for DNA replication.

Both FK506 and rapamycin are potentially useful in the treatment of human disease. FK506 has been approved by the FDA for use in treating the rejection of transplanted organs. A similar use has been envisioned for rapamycin, and its demonstrated activity in organ transplantation and autoimmune animal models indicate a high clinical potential. Rapamycin has been shown to have antitumor activity against B16 melanocarcinoma, colon 26 tumor, EM ependymoblastoma, CD8F1 mammary and colon 38 murine tumors (Sehgal, 1993). Rapamycin has also shown immunosuppressive activity in assays to measure prevention of development of autoimmune adjuvant arthritis, experimental allergic encephalomyelitis and autoimmune uveoretinitis in the rat (Sehgal, 1993).

The biological activity and structural novelty of both rapamycin and FK506 led to a search for their cellular target(s), and the target of both compounds was identified as the plentiful cytoplasmic protein FKBP12 (for FK506 binding protein) of 12 kDa molecular mass. Since FK506 and rapamycin bound to the same target (Kd of 0.4 and 0.2 nM, respectively) and affected different pathways, a new function was attributed to the FKBP12-ligand complex. This new function arises from the ability of FKBP12-FK506 and FKBP12-rapamycin complexes, but not the individual components, to bind to and inhibit still other protein targets. The FKBP12-FK506 complex inhibits the phosphatase activity of calcineurin, a crucial component of the TCR pathway. Calcineurin is a serine/threonine phosphatase also called PP2B. The FKBP12-rapamycin complex inhibits the IL-2R signal by binding to a large (289kDa) protein named FRAP in humans (Brown *et al*, 1994) or RAFT in rats (Sabatini *et al*, 1994; Chiu *et al*, 1994).

The structural basis for the tight binding of FK506 and rapamycin by FKBP12 has been investigated by both X-ray diffraction and NMR techniques (Clardy, 1995). In particular, high resolution X-ray structures are available for FKBP12-FK506 (1.4 Å resolution) and FKBP12-rapamycin (1.7 Å resolution) (Van Duyne *et al*, 1991; Van Duyne *et al*, 1991a; Van Duyne *et al*, 1993). These structures reveal, among other things, the fold of FKBP12, the atomic details of the hydrophobic binding pocket, and the details of how FK506 and rapamycin interact with the binding pocket. A structural analysis of the complex formed between FKBP12-FK506-calcineurin is also available (Griffith *et al*, 1995). That structure reveals how the portion of FK506 not involved in binding FKBP12 interacts with calcineurin and inhibits its phosphatase activity.

The biochemical characterization of FRAP, the target of the FKBP12-rapamycin complex, remains incomplete. The C-terminal domain resembles a phosphatidylinositol (PI) kinase, but to date no PI or protein kinase activity has been convincingly demonstrated. FRAP (RAFT, TOR) are members of a rapidly growing and important family of proteins that have been identified only recently (Zakian, 1995). ATM, TEL1, DNA-PK and MEC1 are some of the recently characterized members of this family of PIK-related kinases. (*See e.g.*, Keith, 1995). ATM (for ataxia telngiectasia mutant) is responsible for a human autosomal hereditary disease characterized by cerebellar degeneration, progressive mental retardation, uneven gait, dilation of blood vessels, immune deficiencies, premature aging and a hundredfold increase in cancer susceptibility (Zakian, 1995). Persons who are heterozygous in ATM are believed to be at elevated risk for cancer. Mutations to TEL1 lead to abnormally short telomeres, and in conjunction with other mutations can lead to sensitivity to X-rays, UV radiation and hydroxyurea. DNA-PK is, as the name suggests, a DNA-dependent protein kinase that recognizes damaged DNA, and human cells without DNA-PK activity are radiation sensitive and repair deficient. MEC1 is required for both S-M and G2-M checkpoint progression as well as for meiotic recombination in yeast. Thus MEC1 is arguably the master checkpoint gene in yeast.

FRAP is a large protein (2549 amino acid residues), and only a small fraction can be involved in recognizing the FKBP12-rapamycin complex. Fortunately all of these residues are in one domain, and this domain, which is called the FKBP12-rapamycin binding (FRB) domain, is the protein used in this invention. It was identified through tryptic digests of FRAP and independently produced as an 11 kDa soluble protein (Chen *et al*, 1995)

Unfortunately, until now, three-dimensional structural details of the association of FKBP12-rapamycin with the FRB domain of FRAP have remained completely unknown. In the absence of such three-dimensional structural details, it has been impossible to design compounds based on that structure which would be capable of mimicking rapamycin's binding to the FRB domain. We have now obtained crystals of that ternary complex and have determined its three dimensional structure. With this information, it is now possible for the first time to rationally design compounds capable of binding to an FRB domain and mimicking the pharmacological activity of rapamycin. Such mimics may be used in place of rapamycin as immunosuppressive agents or in other pharmacological applications.

Summary of the Invention

This invention centers on the FRB domain of human FRAP and begins with obtaining crystals of human FKBP12-rapamycin-FRB of sufficient quality to determine the three dimensional (tertiary) structure of the complex by X-ray diffraction methods.

In considering our work, it should be appreciated that obtaining protein crystals in any case is a somewhat unpredictable art, especially in cases in which the practitioner lacks the guidance of prior successes in preparing and/or crystalizing any closely related proteins. Obtaining our first crystals of the ternary complex was therefore itself an unexpected result. In addition, our data represents the first detailed information available on the three dimensional structure of FRAP or of any of the PIK-related kinases and revealed an unpredicted array of surface features.

Our results are useful in a number of applications. As previously mentioned, the atomic details of how the FKBP12-rapamycin complex interacts with the FRB domain is essential for the structure-based design of rapamycin analogs. As noted above, rapamycin has several promising clinical indications, and improved rapamycin analogs would be useful therapeutic agents. This structure can be used as an essential starting point in predicting, via homology modeling, the structures of related proteins which contain homologous FRB domains, including other members of the PIK-related kinase family.

Furthermore, the structure shows—in atomic detail—how a small organic molecule, rapamycin, can be used to hold two proteins, FKBP12 and FRB, in close proximity. As such, this structure contains important lessons for the design of heterodimerizing agents.

Thus, the knowledge obtained concerning the FRB of FRAP can be used to model the tertiary structure of related proteins. By way of example, the structure of renin has been modeled using the tertiary structure of endothiapepsin as a starting point for the derivation.

Model building of cercarial elastase and tophozoite cysteine protease were each built from known serine and cysteine proteases that have less than 35% sequence identity. The resultant models were used to design inhibitors in the low micromolar range. (*Proc. Natl. Acad. Sci.* **1993**, *90*, 3583). Furthermore, alternative methods of tertiary structure determination that do not rely on X-ray diffraction techniques and thus do not require crystallization of the protein, such as NMR techniques, are simplified if a model of the structure is available for refinement using the additional data gathered by the alternative technique. Thus, knowledge of the tertiary structure of the FRB region of FRAP provides a significant window to the structure of other proteins containing a homologous FRB domain, including the other PIK-related kinases.

Accordingly, one object of this invention is to provide a composition, in crystalline form, comprising a protein containing an FRB domain. The protein may have a bound ligand or may be part of a complex with a second protein molecule and a shared ligand. For instance, the crystalline composition may contain a complex containing a first protein having a peptide sequence derived or selected from that of an FKBP12 protein, *e.g.*, human FKBP12; a second protein having a peptide sequence derived or selected from that of an FRB domain of a PIK-related kinase family member, *e.g.* the FRB domain of human FRAP; and a ligand such as rapamycin which is capable of binding to both proteins to form a ternary complex. Such a crystalline composition may contain one or more heavy atoms, *e.g.*, one or more lead, mercury, gold and/or selenium atoms. Such a heavy atom derivative may be obtained, for example, by expressing a gene encoding the protein of interest under conditions permitting the incorporation of one or more heavy atom labels (*e.g.* as in the incorporation of selenomethionine), reacting the protein with a reagent capable of linking a heavy atom to the protein (*e.g.* trimethyl lead acetate) or soaking a substance containing a heavy atom into the crystals.

Preferred crystalline compositions of this invention are capable of diffracting x-rays to a resolution of better than about 3.5 Å, and more preferably to a resolution of 2.7 Å or better, and are useful for determining the three-dimensional structure of the material. (The smaller the number of angstroms, the better the resolution.)

Crystalline compositions of this invention specifically include those in which the crystals are characterized by the structural coordinates of the FRB protein set forth in the accompanying Appendix I or characterized by coordinates having a root mean square deviation therefrom, with respect to backbone atoms of amino acids listed in Appendix I, of 1.5 Å or less. Furthermore, our crystalline compositions include crystals characterized by the structural coordinates of both the FRB and FKBP12 proteins set forth in Appendix I, optionally including a molecule of rapamycin as defined structurally by the accompanying coordinates therefor.

Structural coordinates of a crystalline composition of this invention may be stored in a machine-readable form on a machine-readable storage medium, *e.g.* a computer hard drive, diskette, DAT tape, etc., for display as a three-dimensional shape or for other uses involving computer-assisted manipulation of, or computation based on, the structural coordinates or the three-dimensional structures they define. For example, data defining the three dimensional

structure of a composition of this invention or a portion thereof containing an FRB domain-containing protein of the PIK-related kinase family, or portions or structurally similar homologues of such proteins, may be stored in a machine-readable storage medium, and may be displayed as a graphical three-dimensional representation of the protein structure, typically using a computer capable of reading the data from said storage medium and programmed with instructions for creating the representation from such data. This invention thus encompasses a machine, such as a computer, having a memory which contains data representing the structural coordinates of a crystalline composition of this invention, *e.g.* the coordinates set forth in Appendix I, together with additional optional data and instructions for manipulating such data. Such data may be used for a variety of purposes, such as the elucidation of other related structures and drug discovery.

A first set of such machine readable data may be combined with a second set of machine-readable data using a machine programmed with instructions for using the first data set and the second data set to determine at least a portion of the coordinates corresponding to the second set of machine-readable data. For instance, the first set of data may comprise a Fourier transform of at least a portion of the coordinates for the complex set forth in Appendix I, while the second data set may comprise X-ray diffraction data of a molecule or molecular complex.

More specifically, one of the objects of this invention is to provide three-dimensional structural information on the FRB domain of FRAP, of other members of the PIK-related kinase family which containg homologous FRB domains, and of homologs or variants thereof, preferably in association with a bound ligand or bound ligand:protein complex (such as FKBP12-rapamycin). To that end, we provide for the use of the structural coordinates of a crystalline composition of this invention, or portions thereof, to solve, *e.g.* by molecular replacement, the three dimensional structure of a crystalline form of another such protein, protein:ligand complex, or protein:ligand:protein complex. Doing so involves obtaining x-ray diffraction data for crystals of the protein or complex for which one wishes to determine the three dimensional structure. Then, one determines the three-dimensional structure of that protein or complex by analyzing the x-ray diffraction data using molecular replacement techniques with reference to the previous structural coordinates. As described in US Patent No. 5,353,236, for instance, molecular replacement uses a molecule having a known structure as a starting point to model the structure of an unknown crystalline sample. This technique is based on the principle that two molecules which have similar structures, orientations and positions in the unit cell diffract similarly. Molecular replacement involves positioning the known structure in the unit cell in the same location and orientation as the unknown structure. Once positioned, the atoms of the known structure in the unit cell are used to calculate the structure factors that would result from a hypothetical diffraction experiment. This involves rotating the known structure in the six dimensions (three angular and three spatial dimensions) until alignment of the known structure with the experimental data is achieved. This approximate structure can be fine-tuned to yield a more accurate and often higher resolution structure using various

refinement techniques. For instance, the resultant model for the structure defined by the experimental data may be subjected to rigid body refinement in which the model is subjected to limited additional rotation in the six dimensions yielding positioning shifts of under about 5%. The refined model may then be further refined using other known refinement methods.

For example, one may use molecular replacement to exploit a set of coordinates such as set forth in Appendix I to determine the structure of a crystalline co-complex of the FRB domain, FKBP12 and a ligand other than rapamycin. Likewise one may use that same approach to determine the three dimensional structure of a complex of FKBP12, rapamycin and a protein containing a modified FRAP FRB domain or an FRB domain from a homolog of FRAP.

Another object of the invention is to provide a method for determining the three-dimensional structure of a protein containing an FRB domain, or a complex of the protein with a ligand therefor, using homology modeling techniques and structural coordinates for a composition of this invention. Homology modeling involves constructing a model of an unknown structure using structural coordinates of one or more related proteins, protein domains and/or subdomains. Homology modeling may be conducted by fitting common or homologous portions of the protein or peptide whose three dimensional structure is to be solved to the three dimensional structure of homologous structural elements. Homology modeling can include rebuilding part or all of a three dimensional structure with replacement of amino acids (or other components) by those of the related structure to be solved. The structural coordinates obtained for the related protein or complex may be stored, displayed, manipulated and otherwise used in like fashion as those for the ternary complex of FKBP12-rapamycin-FRB set forth in Appendix I.

Crystalline compositions of this invention thus provide a starting material, and their three dimensional structure coordinates a point of reference, for use in solving the three-dimensional structure of other proteins containing an FRB domain homologous to that of FRAP, as well as complexes containing such a protein. Sequence similarity may be determined using any conventional similarity matrix. (*See e.g.* Dayhoff,1979; Greer, 1981; and Gonnet, 1992). Proteins containing at least one FRB domain having at least 15% peptide sequence identity or similarity with respect to our FRB, as determined by any of the approaches described above, are considered FRAP homologs for the purpose of this disclosure.

By way of further example, the three dimensional structure defined by the machine readable data for the FRB domain (with or without the FKBP12 component) may be computationally evaluated for its ability to associate with various chemical entities. The term "chemical entity", as used herein, refers to chemical compounds, complexes of at least two chemical compounds, and fragments of such compounds or complexes.

For instance, a first set of machine-readable data defining the 3-D structure of FRAP or a FRAP homolog, or a portion or complex thereof, is combined with a second set of machine-readable data defining the structure of a chemical entity or moiety of interest using a machine programmed with instructions for evaluating the ability of the chemical entity or moiety to

associate with the FRAP or FRAP homolog protein or portion or complex thereof and/or the location and/or orientation of such association. Such methods provide insight into the location, orientation and energetics of association of protein surfaces with such chemical entities.

Chemical entities that are capable of mimicking rapamycin's ability to associate with FRAP or a FRAP homolog should share part or all of rapamycin's pharmacologic activities, *e.g.* immunosuppressive activity, but may be designed for more convenient or economical preparation, improved pharmacokinetics, reduced side effects, etc. Such chemical entities therefore include potential drug candidates.

The three dimensional structure defined by the data may be displayed in a graphical format permitting visual inspection of the structure, as well as visual inspection of the association of the protein component(s) with rapamycin or other chemical entities. Alternatively, more quantitative or computational methods may be used. For example, one method of this invention for evaluating the ability of a chemical entity to associate with any of the molecules or molecular complexes set forth herein comprises the steps of: (a) employing computational means to perform a fitting operation between the chemical entity and a binding pocket or other surface feature of the molecule or molecular complex; and (b) analyzing the results of said fitting operation to quantify the association between the chemical entity and the binding pocket.

This invention further provides for the use of the structural coordinates of a crystalline composition of this invention, or portions thereof, to identify reactive amino acids, such as cysteine residues, within the three-dimensional structure, preferably within or adjacent to a ligand binding site; to generate and visualize a molecular surface, such as a water-accessible surface or a surface comprising the space-filling van der Waals surface of all atoms; to calculate and visualize the size and shape of surface features of the protein or complex, *e.g.*, ligand binding pockets; to locate potential H-bond donors and acceptors within the three-dimensional structure, preferably within or adjacent to a ligand binding site; to calculate regions of hydrophobicity and hydrophilicity within the three-dimensional structure, preferably within or adjacent to a ligand binding site; and to calculate and visualize regions on or adjacent to the protein surface of favorable interaction energies with respect to selected functional groups of interest (*e.g.* amino, hydroxyl, carboxyl, methylene, alkyl, alkenyl, aromatic carbon, aromatic rings, heteroaromatic rings, etc.). One may use the foregoing approaches for characterizing the FRB domain-containing protein and its interactions with moieties of potential ligands to design or select compounds capable of specific covalent attachment to reactive amino acids (*e.g.*, cysteine) and to design or select compounds of complementary characteristics (*e.g.*, size, shape, charge, hydrophobicity/hydrophilicity, ability to participate in hydrogen bonding, etc.) to surface features of the protein, a set of which may be preselected. Using the structural coordinates, one may also predict or calculate the orientation, binding constant or relative affinity of a given ligand to the protein in the complexed state, and use that information to design or select compounds of improved affinity.

In such cases, the structural coordinates of the FRAP or FRAP homolog protein, or portion or complex thereof, are entered in machine readable form into a machine programmed with instructions for carrying out the desired operation and containing any necessary additional data, *e.g.* data defining structural and/or functional characteristics of a potential ligand or moiety thereof, defining molecular characteristics of the various amino acids, etc.

One method of this invention provides for selecting from a database of chemical structures a compound capable of binding to FRAP or a FRAP homolog. The method starts with structural coordinates of a crystalline composition of the invention, *e.g.*, coordinates defining the three dimensional structure of FRAP or a FRAP homolog or a portion thereof or a complex thereof. Points associated with that three dimensional structure are characterized with respect to the favorability of interactions with one or more functional groups. A database of chemical structures is then searched for candidate compounds containing one or more functional groups disposed for favorable interaction with the protein based on the prior characterization. Compounds having structures which best fit the points of favorable interaction with the three dimensional structure are thus identified.

It is often preferred, although not required, that such searching be conducted with the aid of a computer. In that case a first set of machine-readable data defining the 3D structure of a FRAP or FRAP homolog protein, or a portion or protein-ligand complex thereof, is combined with a second set of machine readable data defining one or more moieties or functional groups of interest, using a machine programmed with instructions for identifying preferred locations for favorable interaction between the functional group(s) and atoms of the protein. A third set of data, i.e. data defining the location(s) of favorable interaction between protein and functional group(s) is so generated. That third set of data is then combined with a fourth set of data defining the 3D structures of one or more chemical entities using a machine programmed with instructions for identifying chemical entities containing functional groups so disposed as to best fit the locations of their respective favorable interaction with the protein.

Compounds having the structures selected or designed by any of the foregoing means may be tested for their ability to bind to FRAP or a FRAP homolog, inhibit the binding of FRAP or a FRAP homolog to a natural or non-natural ligand therefor (*e.g.* FKBP12-rapamycin, in the case of FRAP), and/or inhibit a biological function mediated by FRAP or the FRAP homolog.

This invention also permits methods for designing a compound capable of binding to a FRAP or FRAP homolog based on the three dimensional structure of bound rapamycin. One such method involves graphically displaying a three-dimensional representation based on coordinates defining the three-dimensional structure of a FRAP or FRAP homolog protein or a portion thereof complexed with a ligand such as the FKBP12:rapamycin complex. Interactions between portions of ligand and protein are characterized in order to identify candidate moieties of the ligand for replacement. One or more portions of the ligand which interact with the protein may be replaced with substitute moieties selected from a knowledge base of one or more candidate substitute moieties, and/or moieties may be added to the ligand to permit additional

interactions with the protein. Compounds first identified by any of the methods described herein are also encompassed by this invention.

Brief Description of the Drawings

FIG. 1 depicts a computer system.

FIG. 2 depicts storage media of this invention.

FIG. 3 depicts a ribbon diagram of the three dimensional structure of the FKBP12:rapamycin:FRB domain complex, as defined by the coordinates of Appendix I.

Detailed Description of the Invention

Despite the key role played by the FKBP12:rapamycin:FRAP complex in the IL-2/IL-2R signaling pathway, and despite the growing appreciation of the biological importance of the PIK-related kinase family, nothing was known of the three-dimensional architecture by which the FRB domain of FRAP (or of any FRAP homolog) engages the FKBP12:rapamycin complex required for its biological activity. X-ray crystallographic techniques could in principle address such issues. However, notwithstanding the key biological functions mediated by FRAP, there have been no reports disclosing that suitable crystals had been or could be obtained, let alone reports disclosing any x-ray crystallographic data or other information concerning the three-dimensional structure of any FRB domain. Even in the event that crystals had been obtained, then-available three-dimensional structural data relating to the FKBP12:rapamycin complex would not have been been sufficient for solving the ternary complex structure, at least in part, because the initial electron density maps wouldn't have permitted the chain of FRB to be traced. Even if parts of the chain could have been traced, they would not have refined under least-squares minimization techniques.

Nonetheless, we have succeeded in producing FKBP12 and FRAP FRB proteins, and have obtained crystals of their ternary complex with rapamycin. We have solved the three-dimensional structure of the crystalline complex using x-ray diffraction techniques. In view of our successes as disclosed herein, it can now be said that proteins comprising FRB domains can be produced in stable form, purified, and crystallized, and that their three-dimensional structures can be determined, all using materials and methods such as disclosed herein.

As mentioned elsewhere, FRAP is one of a number of PIK-related kinase family members that contain an FRB domain. PIK-related kinase family members share regions of homology including lipid kinase homologous regions, kinase domains and, in at least a number of cases, FRB domains. The presence and boundaries of homologous regions in a protein sequence can be identified by using a computer alignment program that identifies amino acid sequence homology to a known sequence or domain. For example, the FRB domain (amino acids 2015 - 2114) of FRAP may be used for such analysis, but FRB domains from other proteins such as RAPT or TOR1 or TOR2 can be used as well. The alignment method typically used by such programs is the Needleman-Wunch alignment. See *e.g.*, "A General Method Applicable to the Search for

Similarities in the Amino Acid Sequence of Two Proteins." Needlman, S.B.; Wunch, C.D. *J. Mol. Biol.* 1970, *48* , 443-453.

We expressed the FRAP FRB domain as a glutathione-S-transferase (GST) fusion protein. The cDNA encoding residues 2015 - 2114 from human FRAP (Chen *et al*, 1995) was cloned into a pGEX vector and expressed in E coli, the resulting fusion protein was recovered and cleaved to yield the FRB protein which was then purified, all as described in detail below. FKBP12 protein was similarly obtained using a cDNA encoding residues 1 - 107 from human FKBP12 (Standaert *et al*, 1990, Nature 346: 671-674..

Other proteins containing an FRB domain may also be used, including larger FRAP fragments containing the FRB and flanking peptide sequence, including up to the entire FRAP protein. Additionally, FRB proteins can be prepared by analogous means containing homologous FRB regions from other proteins, including RAPT, TOR1, TOR2 or other members of the PIK-related kinase family. It should further be appreciated that other expression systems may be readily employed., including , *e.g.*, materials and methods for expression in *E. coli* using T7, maltose-binding protein fusion (MBP), with epitope tags (His6, HA, myc, Flag) included or cleaved off. Baculoviral expression may be used, *e.g.* using pVL1393 or derivatives, for tFRB domain, fused (or not) to epitope tag or fusion partner such as GST. Conventional materials and methods for expression in mammalian, yeast or other cells may also be used.

Rapamycin may be prepared by known methods or may be obtained from commercial sources. Rapamycin analogs such as disclosed, *e.g.*, in Luengo *et al*, 1995, Chemistry & Biology 2(7):471-481, may be used in place of rapamycin, in forming complexes of this invention.

Complex formation, crystallization, X ray diffraction experiments and interpretation of the diffraction data were conducted as described in detail in the Experimental Examples below. The resulting structural coordinates for a crystalline composition comprising FKBP12:rapamycin:FRB of FRAP (one molecule of complex per asymmetric unit) are set forth in Protein Database format in Appendix I. Solving the X-ray crystal structure of the ternary complex allowed us to conduct the first three dimensional characterization of an FRB:ligand complex (viewing FKBP12:rapamycin as the "ligand"). The complex, depicted in schematic form in FIG. 3, involves an elaborate array of contacts between the two protein domains and their mutual small molecule ligand. This work reveals the first structural insights into an FRB domain-containing protein.

Structure of the Ternary Complex

The ternary complex of FKBP12-rapamycin-FRB has overall dimensions of 60 Å x 45 Å x 35 Å with the rapamycin sandwiched between FKBP12 and FRB. The FKBP12 structure is basically the same as in previously reported binary structures, with a five stranded anti parallel β-sheet and a short α-helix. This binary structure was originally determined in the FKBP12-FK506 complex and later in the FKBP12-rapamycin complex (Van Duyne *et al*, 1993). The four helix bundle of FRB does not wrap around the effector site of FKBP12-rapamycin; it

just touches the effector (i.e., FRB-binding) interface of the binary complex with few protein-protein interactions. All of the interactions between rapamycin and FRB are hydrophobic interactions, and protein-protein interactions between FKBP12 and FRB are limited to the 80s loop and one side chain of the 40s loop of FKBP12 (Table 2). The solvent accessible surface areas of FKBP12 and FRB are 5348 $Å^2$ and 5711 $Å^2$, respectively. Since the solvent accessible surface area of the FKBP12-FRB complex (protein only) is 10342 $Å^2$, binding results in a very modest 6% reduction of solvent accessible surface area. Two long side chains in the 40s loop (Lys44 and Lys47) and three residues in the 80s loop (Thr85, Gly86 and His87) of FKBP12 appear to make crucial contact in the ternary complex. In the FRB site, two residues at the end of α1 and the α1-α2 loop (Arg2042 and Tyr2038) contact the 80s loop of FKBP12, and two residues in helix α4 (Tyr2105 and Asp2102) form direct or water-mediated hydrogen bonds to the 40s loop of FKBP12. The loop-loop interaction between 80s loop (FKBP12) and the α1-α2 loop (FRB) and the loop-helix interaction between 40s loop (FKBP12) and helix α4 are the main protein-protein interactions in this ternary complex and thus contribute all of the protein-protein binding force forming the ternary complex.

Structure of FRB domain of FRAP

The FRB domain of the FRAP forms a typical four helix bundle, which is one of the most common structural motifs in globular proteins. The overall dimensions of this domain are 45 Å x 30 Å x 30 Å. All four helices (termed α1-α4) are connected with short underhand loops. The longest helix α3 (residues 2065-2091) has a bend at residue 2074 of 59°. Except for a small bent part of α3 (residues 1065-2073), all four helices have similar lengths (16-19 residues, about 30 Å in length). The α2 helix also has a small bend around residues Glu2049, Val2050 and Leu2051 to form a 3_{10}-helical turn rather than a normal α-helix. The angle between α1 and α2 is 22° and the angle between α3 and α4 is 20°. The angles between these pairs are in the range of 40-60°, which indicates that this four helix bundle is close to the 'X' type interhelical

Table 2 Intra-molecular hydrogen bonds and close contacts in the ternary complex

Inter-helical interactions in the FRB domain of FRAP

				Distance (Å)
His 2055 (α2)	Nε2	Tyr 2104 (α4)	OH	2.85
His 2028 (α1)	Nε2	Ser 2112 (C terminal)	Oγ	3.23

Close contacts of rapamycin and FRB domain of FRAP

Rapamycin	FRB domain of FRAP		Distance (Å)
C50	Thr 2098	O	3.13
C27	Ser 2035	Oγ	3.39
C51	Ser 2035	Oγ	3.38

Interactions of FKBP12 and FRB domain of FRAP

FKBP12		FRB domain of FRAP		Distance (Å)
Lys 47	O	Tyr 2105	OH	2.56
Thr 85	Oγ1	Arg 2042	NH1	3.10
Thr 85	Oγ1	Arg 2042	NH2	2.88
Gly 86	O	Arg 2042	NH2	2.79
His 87	Nε2	Tyr 2038	OH	*via* H_2O 301
His 87	Nδ1	Arg 2042	NH2	*via* H_2O 303
Lys 44	Nζ	Asp 2102	Oδ1	*via* H_2O 310

pattern which is the alternating pattern of parallel and perpendicular helix-helix interactions (Harris *et al*, 1994). As usual, most of the hydrophobic and aromatic residues are located in the inter-helical interface and most of the hydrophilic residues are in the outside of the bundle, which is exposed to the solvent. Only two strong hydrogen bonds were found for the inter-helical interactions (Table 2) and could be key interactions maintaining the overall conformation of the four helix bundle. Helices α1 and α4 , which have an interhelical angle of 44°, form a deep cleft on the molecular surface of this domain. This cleft is surrounded by six aromatic side chains forming the 'aromatic pocket' which has exquisite steric complementary for the rapamycin effector domain binding.

Structure of FKBP12-rapamycin

The structure of FKBP12 in the ternary complex is basically the same as that in the binary complex of FKBP12-rapamycin or FKBP12-FK506. The protein fold and the architecture of the secondary structure are exactly the same as in the binary complex, and the interaction with rapamycin is also the same as that of the binary complex. The overall r.m.s. deviation between the FKBP12 in the ternary complex and that in the FKBP12-rapamycin complex is 1.14 Å (0.49 Å for the main chain), and the deviation between FKBP12 in the ternary complex and that in the FKBP12-FK506 complex is 1.11 Å (0.48 Å for the main chain), which implies that binding of FKBP12:rapamycin to the FRAP FRB domain is not accompanied by significant changes in the conformation of the FRB binding site on FKBP12 or of the effector domain of rapamycin. Even the 40s loop and 80s loop regions in the FKBP12, that have direct interaction to the FRB domain, are not significantly different in 3D structure from that seen in the binary complexes. These r.m.s. values were calculated by the rigid-body fitting on the main chain atoms in the FKBP12 using QUANTA. The overlay of FKBP12-FK506 to the ternary complex clearly confirmed the fact that FKBP12-FK506 complex can't bind FRAP as FK506's effector region does not extend enough. The protein-protein interactions by themselves between FKBP12 and FRB are not enough for the formation of a binary complex; rapamycin is essential to mediate the interaction of the two proteins.

FKBP12-rapamycin binding to FRAP

While the interactions of rapamycin with FRB are all hydrophobic, rapamycin-FKBP12 interactions employ five hydrogen bonds which are the same found in the binary complex of FKBP12-rapamycin, to govern this interaction. Rapamycin is surrounded by five conserved aromatic residues in FKBP12, which makes the binding pocket for the rapamycin a complete 'aromatic pocket' along with six aromatic residues in FRB domain. Comparing the sequence of these aromatic residues of FRB domain with other FKBP-rapamycin target proteins, these six aromatic residues are all conserved in RAFT (Sabatini *et al*, 1994), TOR1, and TOR2 (Stan, *et al*, 1994)—suggesting that these structural results will be applicable to other members of the PIK-related kinase family. It is expected that binding domains of these other proteins have a similar structure with FRB domain. For the interaction between rapamycin and FRB domain, two major sites on FRB are considered crucial for rapamycin binding. Ser2035, which is also conserved in other FKBP12-rapamycin target proteins, has close contact with C27 and C51 of rapamycin (Table 2). The other site is Thr2098 which has a close contact with C50 of rapamycin. C50 of the rapamycin is at the end of C16 methoxy group, which has been a key target for substituted analogs. All of the hydrophobic interactions between rapamycin and FRB including Ser2035 and Thr2098 can be considered as the main force contributing to complete ternary complex.

Mutational studies

Ser2035 in FRB has been the major site for the site-directed mutation studies of FRAP (Chen *et al*, 1995). Those studies revealed that the substitution of this residue to other residues larger than alanine abolish binding affinity toward FKBP12-rapamycin . The crystal structure of the ternary complex shows the direct effect of steric hindrance when this position is substituted by longer side chains. It has been suggested that this conserved serine site is a phosphorylation site, and phosphorylation would abrogate binding. By the binding of FKBP12-rapamycin, this serine site, which is open to the solvent when unbound, is protected from phosphorylation and this probably causes the inhibition of the downstream of the signaling pathway.

For rapamycin, C16 has been the main site for substitution in published structure-activity studies (Luengo *et al*, 1995). The studies of C16 analogs of rapamycin showed that the bulky group substitutions on this position have lower affinity for the FKBP12 binding and lower activity. However some analogs with different stereochemistry or different groups showed retained activity and affinity to FKBP12. Such C-16 substituted analogs could be of therapeutic use.

Applications of the invention

This invention encompasses crystalline compositions containing FRAP or a FRAP homolog protein or portion thereof having a region characterized by structural coordinates of the FRB domain set forth in Appendix I, or by coordinates having a root mean square deviation

therefrom of less than about 1.5 Å, preferably less than about 1 Å, and even more preferably less than about 0.5 Å, with respect to backbone atoms of amino acid residues listed there.

As practitioners in this art will appreciate, various computational analyses may be used to determine the degree of similarity between the three dimensional structure of a given protein (or a portion or complex thereof) and FRAP or a FRAP homolog protein or portion (*e.g.* the FRB domain) or complex thereof such as are described herein. Such analyses may be carried out with commercially available software applications, such as the Molecular Similarity application of QUANTA (Molecular Simulations Inc., Waltham, MA) version 3.3, and as described in the accompanying User's Guide, Volume 3 pgs. 134 - 135.

The Molecular Similarity application permits comparisons between different structures, different conformations of the same structure, and different parts of the same structure. The procedure used in Molecular Similarity to compare structures is divided into four steps: (1) load the structures to be compared; (2) define the atom equivalences in these structures; (3) perform a fitting operation; and (4) analyze the results.

Each structure is identified by a name. One structure is identified as the target (i.e., the fixed structure); all remaining structures are working structures (i.e., moving structures). Since atom equivalency within QUANTA is defined by user input, for the purpose of this invention we define equivalent atoms as protein backbone atoms (N, Cα, C and O) for all conserved residues between the two structures being compared and consider only rigid fitting operations.

When a rigid fitting method is used, the working structure is translated and rotated to obtain an optimum fit with the target structure. The fitting operation uses a least squares fitting algorithm that computes the optimum translation and rotation to be applied to the moving structure, such that the root mean square difference of the fit over the specified pairs of equivalent atom is an absolute minimum. This number, given in angstroms, is reported by QUANTA.

For the purpose of this invention, any set of structural coordinates of a FRAP or FRAP homolog protein, portion of a FRAP or FRAP homolog protein or molecular complex thereof that has a root mean square deviation of conserved residue backbone atoms (N, Cα, C, O) of less than 1.5Å when superimposed—using backbone atoms—on the relevant structural coordinates of a protein or complex of this invention, *e.g.* the coordinates listed in Appendix I, are considered identical. More preferably, the root mean square deviation is less than 1.0Å. Most preferably, the root mean square deviation is less than 0.5Å.

The term "root mean square deviation" means the square root of the arithmetic mean of the squares of the deviations from the mean. It is a way to express the deviation or variation from a trend or object. For purposes of this invention, the "root mean square deviation" defines the variation in the backbone of a protein from the backbone of a protein of this invention, such as the FRB of FRAP, as defined by the structural coordinates of Appendix I and described herein.

The term "least squares" refers to a method based on the principle that the best estimate of a value is that in which the sum of the squares of the deviations of observed values is a minimum.

In order to use the structural coordinates generated for a crystalline substance of this invention, *e.g.* the structural coordinates of the FRB of FRAP set forth in Appendix I, it is often necessary or desirable to display them as, or convert them to, a three-dimensional shape, or to otherwise manipulate them. This is typically accomplished by the use of commercially available software such as a program which is capable of generating three-dimensional graphical representations of molecules or portions thereof from a set of structural coordinates.

By way of illustration, a non-exclusive list of computer programs for viewing or otherwise manipulating protein structures include the following:

Midas (Univ. of California, San Francisco)
MidasPlus (Univ. of Cal., San Francisco)
MOIL (Univeristy of Illinois)
Yummie (Yale University)
Sybyl (Tripos, Inc.)
Insight/Discover (Biosym Technologies)
MacroModel (Columbia University)
Quanta (Molecular Simulations, Inc.)
Cerius (Molecular Simulations, Inc.)
Alchemy (Tripos, Inc.)
LabVision (Tripos, Inc.)
Rasmol (Glaxo Research and Development)
Ribbon (University of Alabama)
NAOMI (Oxford University)
Explorer Eyechem (Silicon Graphics, Inc.)
Univision (Cray Research)
Molscript (Uppsala University)
Chem-3D (Cambridge Scientific)
Chain (Baylor College of Medicine)
O (Uppsala University)
GRASP (Columbia University)
X-Plor
(Molecular Simulations, Inc.; Yale Univ.)
Spartan (Wavefunction, Inc.)
Catalyst (Molecular Simulations, Inc.)
Molcadd (Tripos, Inc.)
VMD (Univ.of Illinois/Beckman Institute)
Sculpt (Interactive Simulations, Inc.)
Procheck (Brookhaven Nat'l Laboratory)
DGEOM (QCPE)
RE_VIEW (Brunel University)
Modeller (Birbeck Col., Univ. of London)
Xmol (Minnesota Supercomputing Center)
Protein Expert (Cambridge Scientific)
HyperChem (Hypercube)
MD Display (University of Washington)
PKB
(Nat'l Center for Biotech. Info., NIH)
ChemX (Chemical Design, Ltd.)
Cameleon (Oxford Molecular, Inc.)
Iditis (Oxford Molecular, Inc.)

For storage, transfer and use with such programs of structural coordinates for a crystalline substance of this invention, a machine-readable storage medium is provided comprising a data storage material encoded with machine readable data which, when using a machine programmed with instructions for using said data, *e.g.* a computer loaded with one or more programs of the sort identified above, is capable of displaying a graphical three-

dimensional representation of any of the molecules or molecular complexes described herein. Machine-readable storage media comprising a data storage material include conventional computer hard drives, floppy disks, DAT tape, CD-ROM, and other magnetic, magneto-optical, optical, floptical and other media which may be adapted for use with a computer.

Even more preferred is a machine-readable data storage medium that is capable of displaying a graphical three-dimensional representation of a molecule or molecular complex that is defined by the structural coordinates of a complex, FRB-containing protein component thereof, or portion thereof, comprising structural coordinates of an FRB domain such as the FRAP FRB coordinates set forth in our attached Appendix I ± a root mean square deviation from the conserved backbone atoms of the amino acids thereof of not more than 1.5 Å. An illustrative embodiment of this aspect of the invention is a conventional 3.5" diskette, DAT tape or hard drive encoded with a data set, preferably in PDB format, comprising the coordinates of our Appendix I. FIG. 3 illustrates a print-out of a graphical three-dimensional representation of such a complex.

In another embodiment, the machine-readable data storage medium comprises a data storage material encoded with a first set of machine readable data which comprises the Fourier transform of the structural coordinates set forth in Appendix I (or again, a derivative thereof), and which, when using a machine programmed with instructions for using said data, can be combined with a second set of machine readable data comprising the X-ray diffraction pattern of a molecule or molecular complex to determine at least a portion of the structural coordinates corresponding to the second set of machine readable data.

FIG. 1 illustrates one version of these embodiments. The depicted system includes a computer A comprising a central processing unit ("CPU"), a working memory which may be, *e.g.*, RAM (random-access memory) or "core" memory, mass storage memory (such as one or more disk drives or CD-ROM drives), one or more cathode-ray tube ("CRT") display terminals, one or more keyboards, one or more input lines (IP), and one or more output lines (OP), all of which are interconnected by a conventional bidirectional system bus.

Input hardware B, coupled to computer A by input lines, may be implemented in a variety of ways. Machine-readable data of this invention may be inputted via the use of a modem or modems connected by a telephone line or dedicated data line L. Alternatively or additionally, the input hardware may comprise CD-ROM drives or disk drives D. In conjunction with the CRT display terminal, a keyboard may also be used as an input device.

Output hardware, coupled to computer A by output lines, may similarly be implemented by conventional devices. By way of example, output hardware may include a CRT display terminal for displaying a graphical representation of a protein of this invention (or portion thereof) using a program such as QUANTA as described herein. Output hardware might also include a printer, so that hard copy output may be produced, or a disk drive, to store system output for later use.

In operation, the CPU coordinates the use of the various input and output devices, coordinates data accesses from mass storage and accesses to and from working memory, and determines the sequence of data processing steps. A number of programs may be used to process the machine-readable data of this invention. Examples of such programs are discussed in reference to the computational methods of drug discovery as described herein. Specific references to components of the hardware system of FIG. 1 are included as appropriate throughout the following description of the data storage medium.

FIG. 2A shows a cross section of a magnetic data storage medium 100 which can be encoded with a machine-readable data that can be carried out by a system such as a system of FIG. 1. Medium 100 can be a conventional floppy diskette or hard disk, having a suitable substrate 101, which may be conventional, and a suitable coating 102, which may be conventional, on one or both sides, containing magnetic domains (not visible) whose polarity or orientation can be altered magnetically. Medium 100 may also have an opening (not shown) for receiving the spindle of a disk drive or other data storage device 24.

The magnetic domains of coating 102 of medium 100 are polarized or oriented so as to encode in a manner which may be conventional, machine readable data such as that described herein, for execution by a system such as a system of FIG. 1.

FIG. 2B shows a cross section of an optically-readable data storage medium 110 which also can be encoded with such machine-readable data, or set of instructions, which can be carried out by a system such as a system of FIG. 1. Medium 110 can be a conventional compact disk read only memory (CD-ROM) or a rewritable medium such as a magneto-optical disk which is optically readable and magneto-optically writable. Medium 100 preferably has a suitable substrate 111, which may be conventional, and a suitable coating 112, which may be conventional, usually of one side of substrate 111.

In the case of CD-ROM, coating 112 is reflective and is impressed with a plurality of pits 113 to encode the machine-readable data. The arrangement of pits is read by reflecting laser light off the surface of coating 112. A protective coating 114, which preferably is substantially transparent, is provided on top of coating 112.

In the case of a magneto-optical disk, coating 112 has no pits 113, but has a plurality of magnetic domains whose polarity or orientation can be changed magnetically when heated above a certain temperature, as by a laser (not shown). The orientation of the domains can be read by measuring the polarization of laser light reflected from coating 112. The arrangement of the domains encodes the data as described above.

Use of Structure in Drug Discovery

The availability of the three-dimensional structure of the ternary complex of FKBP12:rapamycin:FRB of FRAP makes structure-based drug discovery approaches possible. Structure-based approaches include *de Novo* molecular design, computer-aided optimization of

lead molecules, and computer-based selection of candidate drug structures based on structural criteria.

Rapamycin mimetics may be developed from the bound conformation of rapamycin by design, by searching databases for replacements of one or more structural segments of rapamycin, or by enhancement of existing ligand-protein interactions (i.e., by replacing a component moiety of a ligand with a substitute moiety capable of greater interaction with the target protein, whether through accessible protein contact points or by extrusion of otherwise sequestered waters). Knowledge of the bound conformation of a ligand can suggest avenues for conformational restriction and replacement of atoms and/or bonds of rapamycin. A less biased approach involves computer algorithms for searching databases of three dimensional structures to identify replacements for one or more portions of the ligand. By this method, one can generate compounds for which the bioactive conformation is heavily populated, i.e., compounds which are based on particularly biologically relevant conformations of the ligand. Algorithms for this purpose are implemented in programs such as Cast-3D (Chemical Abstracts Service), 3DB Unity (Tripos, Inc.), Quest-3D (Cambridge Crystallographic Data Center), and MACCS/ISIS-3D (Molecular Design Limited). These geometric searches can be augmented by steric searching, in which the size and shape requirements of the binding site are used to weed out hits that have prohibitive dimensions. Programs that may be used to synchronize the geometric and steric requirements in a search applied to the FRB of FRAP include CAVEAT (P. Bartlett, University of California, Berkeley), HOOK (MSI), ALADDIN (Daylight Software) and DOCK (I.D. Kuntz, University of California, San Francisco; see *e.g.* http://www.cmpharm.ucsf.edu/kuntz-/kuntz.html and references cited therein). All of these searching protocols may be used in conjunction with existing corporate databases, the Cambridge Structural Database, or available chemical databases from chemical suppliers.

Characterization of Compounds

Compounds designed, selected and/or optimized by methods described above may be evaluated for binding activity with respect to proteins containing one or more FRB domains using various approaches, a number of which are well known in the art. For instance, compounds may be evaluated for activity as competitive inhibitors of the binding of a natural ligand for the FRB, *e.g.* FKBP12:rapamycin in the case of the FRAP FRB. Competitive inhibition may be determined using any of the numerous available technologies known in the art.

Such compounds may be further evaluated for activity in inhibiting cellular or other biological events mediated by a pathway involving the interaction of interest using a suitable cell-based assay or an animal model. Cell-based assays and animal models suitable for evaluating inhibitory actvity of a compound with respect to a wide variety of cellular and other biological events are known in the art. New assays and models are regularly developed and reported in the scientific literature.

For example, compounds which mimic the binding of rapamycin or FKBP12:rapamycin with respect to FRAP may be evaluated for biological activity in the mouse spelocyte mitogenesis assay or the high-flux yeast-based assay of Luengo *et al, supra*. A battery of *in vivo* models may be used to profile the breadth of the compound's immunosuppressive (or other) activity and compare the profile to those of positive controls such as rapamycin itself. Comparisons may also be made to other currently accepted immunosuppressive compounds, *e.g.* cyclophosphamide, and leflunomide. Initial *in vivo* screening models include: Delayed type hypersensitivity testing, Allogeneic skin transplantation, and Popliteal lymph node hyperplasia. Compounds demonstrating optimal profiles in the above models are advanced into more sophisticated models designed to confirm immunosuppressive activity in specific therapeutic areas including: Rheumatoid arthritis, Transplantation, Graft vs. host disease, and Asthma.

By way of further illustration, compounds may be evaluated in relevant conventional *in vitro* and *in vivo* assays for inhibition of the initiation, maintenance or spread of cancerous growth. See *e.g.*, Ishii *et al.*, J. Antibiot. XLII:1877-1878 (1989) (*in vitro* evaluation of cytotoxic/antitumor activity); Sun *et al*, US Patent 5,206,249 (issued 27 April 1993)(*in vitro* evaluation of growth inhibitory activity on cultured leukemia cells); and Sun *et al, supra* (xenograft models using various human tumor cell lines xenografted into mice, as well as various transgenic animal models).

Single and multiple (*e.g.*, 5 to 7 days) dose investigative toxicology studies are typically performed in the efficacy test species using the intended route of administration for the efficacy study. These investigative toxicology studies are performed to identify maximum tolerated dose, subjective bioavailability from the intraperitoneal or oral routes of administration , and estimation of an initial safety margin. Initial bioavailability and pharmacokinetics (blood clearance) of the compounds may be determined, with standard cold or radioactive assay methods, to assist in defining appropriate dosing regimens for the compounds in the animal models.

Pharmaceutical Compositions and Uses of rapamycin mimetics and other FRAP-binding compounds

Compounds which bind to an FRB domain may be used as biological reagents in binding assays as described herein for functional classification of members of the PIK-related kinase family, particularly newly discovered proteins, based on ligand specificity.

Moreover, compounds identified as described above can be used for their immunosuppressive or other pharmacologic activity in place of rapamycin.

A compound selected or identified in accordance with this invention can be formulated into a pharmaceutical composition containing a pharmaceutically acceptable carrier and/or other excipient(s) using conventional materials and means. Such a composition can be administered as an immunosuppresant, for example, to an animal, either human or non-human. Administration of such composition may be by any conventional route (parenteral, oral, inhalation, and the like) using appropriate formulations as are well known in this art. The

compound can be employed in admixture with conventional excipients, i.e., pharmaceutically acceptable organic or inorganic carrier substances suitable for parenteral administration.

Pharmaceutical applications

By virtue of its capacity to mimic the interaction of rapamycin with FRAP, a compound identified as described herein may be used in pharmaceutical compositions and methods for treatment or prevention of various diseases and disorders in a mammal in need thereof.

Mammals include rodents such as mice, rats and guinea pigs as well as dogs, cats, horses, cattle, sheep, non-human primates and humans.

The preferred method of such treatment or prevention is by administering to a mammal an effective amount of the compound to prevent, alleviate or cure said disease or disorder. Such effective amounts can be readily determined by evaluating the compounds of this invention in conventional assays well-known in the art, including assays described herein.

Therapeutic/Prophylactic Administration & Pharmaceutical Compositions

The invention provides methods of treating, preventing and/or alleviating the symptoms and/or severity of an untoward immune response or other disease or disorder referred to above by administration to a subject of a in an amount effective therefor. The subject will be an animal, including but not limited to animals such as cows, pigs, chickens, *etc.*, and is preferably a mammal, and most preferably human.

Various delivery systems are known and can be used to administer the compound, *e.g.*, encapsulation in liposomes, microparticles, microcapsules, *etc.* One mode of delivery of interest is via pulmonary administration, as detailed more fully *infra*. Other methods of introduction include but are not limited to intradermal, intramuscular, intraperitoneal, intravenous, subcutaneous, intranasal, epidural and oral routes. The compound may be administered by any convenient route, for example by infusion or bolus injection, by absorption through epithelial or mucocutaneous linings (*e.g.*, oral mucosa, rectal and intestinal mucosa, *etc.*) and may be administered together with other biologically active agents. Administration can be systemic or local. For treatment or prophylaxis of nasal, bronchial or pulmonary conditions, preferred routes of administration are oral, nasal or via a bronchial aerosol or nebulizer.

In specific embodiments, it may thus be desirable to administer the compound locally to the area in need of treatment; this may be achieved by, for example, and not by way of limitation, local infusion during surgery, topical application, by injection, by means of a catheter, by means of a suppository, or by means of a skin patch or implant, said implant being of a porous, non-porous, or gelatinous material, including membranes, such as sialastic membranes, or fibers.

This invention also provides pharmaceutical compositions. Such compositions comprise a therapeutically (or prophylactically) effective amount of the compound, and a pharmaceutically acceptable carrier or excipient. Such a carrier includes but is not limited to

saline, buffered saline, dextrose, water, glycerol, ethanol, and combinations thereof. The carrier and composition can be sterile. The formulation should suit the mode of administration.

The composition, if desired, can also contain minor amounts of wetting or emulsifying agents, or pH buffering agents. The composition can be a liquid solution, suspension, emulsion, tablet, pill, capsule, sustained release formulation, or powder. The composition can be formulated as a suppository, with traditional binders and carriers such as triglycerides. Oral formulation can include standard carriers such as pharmaceutical grades of mannitol, lactose, starch, magnesium stearate, sodium saccharine, cellulose, magnesium carbonate, *etc.*

In a specific embodiment, the composition is formulated in accordance with routine procedures as a pharmaceutical composition adapted for intravenous administration to human beings. Typically, compositions for intravenous administration are solutions in sterile isotonic aqueous buffer. Where necessary, the composition may also include a solubilizing agent and a local anesthetic to ease pain at the side of the injection. Generally, the ingredients are supplied either separately or mixed together in unit dosage form, for example, as a lyophilized powder or water free concentrate in a hermetically sealed container such as an ampoule or sachette indicating the quantity of active agent. Where the composition is to be administered by infusion, it can be dispensed with an infusion bottle containing sterile pharmaceutical grade water or saline. Where the composition is administered by injection, an ampoule of sterile water for injection or saline can be provided so that the ingredients may be mixed prior to administration.

Administration to an individual of an effective amount of the compound can also be accomplished topically by administering the compound(s) directly to the affected area of the skin of the individual. For this purpose, the compound is administered or applied in a composition including a pharmacologically acceptable topical carrier, such as a gel, an ointment, a lotion, or a cream, which includes, without limitation, such carriers as water, glycerol, alcohol, propylene glycol, fatty alcohols, triglycerides, fatty acid esters, or mineral oils.

Other topical carriers include liquid petroleum, isopropyl palmitate, polyethylene glycol, ethanol (95%), polyoxyethylene monolaurate (5%) in water, or sodium lauryl sulfate (5%) in water. Other materials such as anti-oxidants, humectants, viscosity stabilizers, and similar agents may be added as necessary.

In addition, in certain instances, it is expected that the compound may be disposed within devices placed upon, in, or under the skin. Such devices include patches, implants, and injections which release the compound into the skin, by either passive or active release mechanisms.

Materials and methods for producing the various formulations are well known in the art [see *e.g.* US Patent Nos. 5,182,293 and 4,837,311 (tablets, capsules and other oral formulations as well as intravenous formulations)].

The effective dose of the compound will typically be in the range of about 0.01 to about 50 mg/kgs, preferably about 0.1 to about 10 mg/kg of mammalian body weight, administered

in single or multiple doses. Generally, the compound may be administered to patients in need of such treatment in a daily dose range of about 1 to about 2000 mg per patient.

The amount of the compound which will be effective in the treatment or prevention of a particular disorder or condition will depend on the nature of the disorder or condition, and can be determined by standard clinical techniques. In addition, *in vitro* or *in vivo* assays may optionally be employed to help identify optimal dosage ranges. Effective doses may be extrapolated from dose-response curves derived from *in vitro* or animal model test systems. The precise dosage level of the compound, as the active component(s), should be determined as in the case of all pharmaceutical treatments, by the attending physician or other health care provider and will depend upon well known factors, including route of administration, and the age, body weight, sex and general health of the individual; the nature, severity and clinical stage of the disease; and the use (or not) of concomitant therapies.

The invention also provides a pharmaceutical pack or kit comprising one or more containers filled with one or more of the ingredients of the pharmaceutical compositions of the invention. Optionally associated with such container(s) can be a notice in the form prescribed by a governmental agency regulating the manufacture, use or sale of pharmaceutical or biological products, which notice reflects approval by the agency of manufacture, use or sale for human administration.

Pulmonary Administration

In one embodiment of this invention, the compound is administered by pulmonary administration, *e.g.* via aerosolization. This route of administration may be particularly useful for treatment or prophylaxis of bronchial or pulmonary infection or tumors.

Pulmonary administration can be accomplished, for example, using any of various delivery devices known in the art (see *e.g.*, Newman, S.P., 1984, in Aerosols and the Lung , Clarke and Davia (eds.), Butterworths, London, England, pp. 197-224; PCT Publication No. WO 92/16192 dated October 1, 1992; PCT Publication No. WO 91/08760 dated June 27, 1991; NTIS Patent Application 7-504-047 filed April 3, 1990 by Roosdorp and Crystal), including but not limited to nebulizers, metered dose inhalers, and powder inhalers. Various delivery devices are commercially available and can be employed, *e.g.*, Ultravent nebulizer (Mallinckrodt, Inc., St. Louis, Missouri); Acorn II nebulizer (Marquest Medical Products, Englewood, Colorado), Ventolin metered dose inhaler (Glaxo Inc., Research Triangle Park, North Carolina); Spinhaler powder inhaler (Fisons Corp., Bedford, Massachusetts) or Turbohaler (Astra). Such devices typically entail the use of formulations suitable for dispensing from such a device, in which a propellant material may be present.

Ultrasonic nebulizers tend to be more efficient than jet nebulizers in producing an aerosol of respirable size from a liquid (Smith and Spino, "Pharmacokinetics of Drugs in Cystic Fibrosis," Consensus Conference, Clinical Outcomes for Evaluation of New CF Therapies, Rockville, Maryland, December 10-11, 1992, Cystic Fibrosis Foundation).

A nebulizer may be used to produce aerosol particles, or any of various physiologically acceptable inert gases may be used as an aerosolizing agent. Other components such as physiologically acceptable surfactants (*e.g.*, glycerides), excipients (*e.g.*, lactose), carriers, and diluents may also be included.

This invention is not to be limited in scope by the specific embodiments described herein. Indeed, various modifications of the invention in addition to those described herein will become apparent to those skilled in the art from the foregoing description. Such modifications are intended to fall within the the scope of the appended claims.

Various patents, patent applications and publications are cited herein, the disclosures of which are incorporated by reference in their entireties.

Experimental Examples

I. Protein Preparation

cDNAs encoding human FKBP12 (Standaert *et al*, 1990) and the 12-kDa FRAP fragment containing the FRB domain (Chen *et al*, 1995) (FRAP12) were subcloned into pGEX-2T (Pharmacia) for the expression of GST-FKBP12 and GST-FRAP12 fusion proteins in *E.coli* strain BL21. Typically, a 2-liter culture was grown to OD_{600}~0.6 at 30 °C and induced with 0.3 mM IPTG at room temperature for 6 hours. Purification and thrombin cleavage of the fusion proteins were performed according to standard procedures (manual from Pharmacia). After removal of free GST, the samples containing FKBP12 or FRAP12 were concentrated to ~10 mL in a 50 mL stir-cell ultraconcentrator (Amicon) with a 3-kDa cutoff filter, and fractionated on a Sephacryl S-100 column (2.5 cm x 85 cm) equilibrated in 10 mM phosphate buffer (pH 7.4) containing 136 mM NaCl, 3 mM KCl, 1 mM DTT. Fractions containing pure FKBP12 or FRAP12 (>95% purity judged by SDS-PAGE) were combined and concentrated to ~10 mg/mL using a stir-cell ultraconcentrator. The concentrated samples were stored in the same phosphate buffer at 4 °C.

II. Crystallization & Structure Determination

Crystallization

Recombinant human FKBP12 purified from *E. coli* was used at 10 mg/mL in 10 mM tris-HCl pH 8.0. Rapamycin was dissolved in methanol and mixed with FKBP12 in a 2:1 molar ratio. The mixture was lightly vortexed and stored overnight at 4°C to insure complete complex formation. Purified 12-kDa FRB domain of FRAP at 10 mg/mL in 50 mM tris-HCl pH 8.0 was added to this mixture in a 1:1 (FKBP12-rapamycin complex:FRB domain) molar ratio. This mixture was also lightly vortexed and let sit overnight at 4°C to insure complete complex formation. Crystallization conditions were screened using the hanging drop method, and rectangular rod-shaped crystals were obtained using: 20% PEG 8000, 10% MPD and 10 mM tris-HCl at pH 8.5. For the hanging drop method, drops of 4µL containing 2µL of complex solution and 2µL of reservoir solution were equilibrated against 0.5 mL of the reservoir solution.

Micro-seeding techniques were used to prepare additional crystals. The initial crystals were crushed and diluted to prepare a seed solution that was added to newly prepared drops. After two weeks, a shower of tiny crystals was obtained. Macro-seeding techniques were then applied to get large crystals suitable for X-ray diffraction. A tiny but well-formed crystal was picked and used as a crystallization seed. After two to three weeks, rectangular rod-shaped crystals with a maximum size of 0.3 x 0.2 x 0.1 mm^3 were obtained, and these crystals were suitable for data collection. The Hg-derivative crystal was obtained by soaking the native crystal in 2 mM $HgCl_2$ solution overnight. All of the crystallization experiments were done at 4°C.

Data Collection

All data sets were collected at room temperature on a San Diego multiwire area detector system mounted on a Rigaku RU-200 rotating anode X-ray source operating at 50 kV and 150mA. The detector was positioned at a 20-value of -30° with a 544 mm detector-crystal distance for the high resolution data and 12° with a 506 mm detector-crystal distance for the low resolution data. The data collection was performed using an ω-scan with an increment of 0.10° for each frame and 40 second exposure time per frame. Crystals belong to the orthorhombic space group $P2_12_12_1$ with unit-cell dimension of a=44.63, b=52.14, c=102.53 Å and one FKBP12-rapamycin-FRB complex in the asymmetric unit. Hg-derivative crystal data were collected under the same conditions. For the native data set, the measured intensity data were processed using SCALEPACK (Otwinski *et al*, 1992) giving 6920 unique reflections out of 43447 measured reflections to 2.7 Å resolution (98.5% data coverage) with R_{sym} of 7.1%. For the Hg-derivative data set, the number of unique reflection was 6884 out of 42681 measured reflections to 2.7 Å (98.0% data coverage), with R_{sym} of 7.1%.

Structure determination

The crystal structure of the ternary complex was solved using the molecular replacement (MR) method combined with the single isomorphous replacement with anomalous scattering (SIRAS) method. Initial phases were obtained from the molecular replacement search using the FKBP12-rapamycin complex structure as a search model. The cross rotation search revealed a clear peak at Θ_1=10.8°, Θ_2=70.0°, Θ_3=309.4° with height/r.m.s. ratio of 12.9 and the translation search also showed a clear peak at x=0.000, y=0.230, z=0.417 with height/r.m.s. ratio of 10.5. Rigid body refinement resulted in an R factor of 0.449 (10-2.7 Å). All molecular replacement calculations used the X-PLOR program (Brunger, 1990). However, the resulting difference electron density map was noisy and hard to interpret. In order to improve the map quality, an Hg derivative crystal was obtained. These data were compared with the native data to give an R_{diff} of 12.7%. Two heavy atom sites were found from the difference Patterson map and were refined using the program PHASES (Furey *et al*,1990). One Hg is bound to Cys22 of FKBP12 with full occupancy - the same Hg site seen in the FKBP12-FK506 complex.

The other heavy atom site is in the middle of FRB domain where it is bound to Cys2085 of FRAP with an occupancy factor of 0.6. Both Patterson-deduced heavy atom positions were validated in the Fo-Fc difference map using Fo of the heavy atom derivative and Fc from the molecular replacement solution. Anomalous dispersion measurements were included in this data set and 16 cycles of a solvent flattening procedure were applied, resulting in a phasing power of 2.76 and mean figure of merit of 0.840. All of these calculations were performed using the program PHASES. The electron density map was calculated using the combined phase from the SIRAS and the molecular replacement solution, which clearly showed four helix bundle architecture of FRB domain of FRAP.

Model Building and refinement

The FKBP12-rapamycin part was well defined in the initial electron density map; only minor changes in the backbone of 30s loop and some side chains were enough to fit the model of FKBP12-rapamycin structure to this electron density map. For the FRB domain part, most of a polyalanine chain could be traced for the helix regions in the initial map. After several cycles of the positional refinement using X-PLOR, loop regions could be traced and the amino acid sequence could be assigned. The program CHAIN (Sack, 1988) was used for the model fitting and building the ternary complex. A total of 95 residues were built for the FRB domain of FRAP; three residues in the N-terminal and two residues in the C-terminal of FRB domain had no electron density and were not included. Positional refinement was followed by simulated annealing (slow cooling from 3000K to 300K in 25 K steps, 0.0005 ps per step and 50 total steps were used in the simulation at each temperature) and restrained B-factor refinement. All refinements were done using the X-PLOR package. Solvent molecules were assigned during the iterative positional and B-factor refinement procedure, if they appeared at the 3.5 σ level of Fo-Fc map, showed good hydrogen bonding geometry and had a low B-factor (less than 50 $Å^2$). The current structure includes 202 amino acids (107 for FKBP12 and 95 for FRB domain), one rapamycin, and 23 water molecules. The final R factor is 19.3% with an R_{free} of 29.9%. The free R-factor is calculated with 10% of the data that were selected at the beginning of the analysis. Crystallographic statistics are summarized in Table 1.

Quality of the coordinates

The final coordinates have good geometry and r.m.s. deviations from the ideality are 0.008 Å for bond lengths and 1.5° for bond angles. Examined by the program PROCHECK (Laskowski, 1993), the current 2.7 Å resolution structure shows that the main-chain and side-chain geometrical parameters are better than expected at this resolution with an overall G-factor of 0.0. Ramachandran plots of ϕ, ψ, angles showed that 86% of the nonglycine and nonproline residues are in energetically most favored regions. The average temperature factors for total atoms and main-chain atoms are 17.0 and 14.7 $Å^2$ respectively. The r.m.s. variation

in the B-factor of bonded atoms is 2.5 $Å^2$. The Luzzati plot (Luzzati, 1952) indicates that the average coordinate error of this complex structure is between 0.25 and 0.30 Å.

Those structural coordinates are set forth in Protein Databank format in Appendix I, below. Such data may be transferred to any desired medium, and formatted as desired, for the practitioner's computer.

This invention encompasses those coordinates as well as any translation or rotation or the like thereof which maintains the internal coordinates, i.e., which maintains their intrinsic, internal relationship. Those skilled in the art will appreciate that the coordinates may be subjected to other transformations including, *e.g.* molecular mechanics calculations such as dynamic simulation, minimization, etc. This invention further encompasses the use of coordinates of the FRB of FRAP, of the ternary complex, or of the corresponding region of FRAP homologs, and in particular, the coordinates set forth in Appendix I, in conducting such transformations (or more extensive transformations such as the generation of alternative conformations), as well as the products of such transformations (i.e., derivatives of the coordinates).

Table 1 Crystallographic statistics of the ternary complex FKBP12-rapamycin-FRB domain of FRAP

Data collection statistics

Data Set	Resolution (Å)	No. of reflections Measured	Unique	Data coverage(%)	R_{sym}(%)*
Native	2.7	43447	6920	98.5	7.1
$HgCl_2$	2.7	42681	6884	98.0	7.1

Molecular replacement results

Rotation function	Θ_1=10.82°	Θ_2=70.00°	Θ_3=309.35°	Height/r.m.s.=12.9σ
Translation function	x=0.000	y=0.230	z=0.417	Height/r.m.s.=10.5σ

Heavy atom data statistics (SIRAS)

Sites	R_{diff}(%)†	Phasing power ◊	Mean figure-of-merit
2	12.7	2.76	0.840

Refinement statistics

Resolution (Å)	Reflections (with |F|>3σ)	Number of atoms	R-factor (%)	R_{free} (%)	R.M.S. deviation Bond lengths (Å)	Bond angles (°)
8-2.7	6206	1727	19.3	29.9	0.008	1.48

*$R_{sym}=\Sigma|\ I-<I>\ |/\Sigma\ I$, where I is the observed intensity and <I> is the average intensity from multiple measurement.

†$R_{diff}=\Sigma\ |F_{PH}-F_P|\ /\Sigma F_{PH}$, where F_P and F_{PH} are the amplitudes of native and derivative structure factors, respectively.

◊Phasing power=r.m.s.(F_H/ε), where F_H is heavy-atom structure factor amplitude and ε is residual lack of closure error.

III. Assays

Compounds which bind to the FRB of FRAP may be evaluated using materials and methods useful for testing the biological or pharmacological activity of rapamycin analogs. See *e.g.* Luengo *et al*, 1995. In addition, the following animal models may be used for further evaluation of such compounds:

(a) DELAYED TYPE HYPERSENSITIVITY

Mouse abdomens are painted with sensitizing chemicals (sensitization) such as dinitroflourobenzene or oxazalone. Seven days later the ears of sensitized mice are painted (challenge) with a lower concentration of the compound. Antigen processing and presentation, T lymphocyte activation, leukocyte infiltration, humoral mediator release, increased microvascular permeability, and plasma exudation all result from challenge of sensitized mice and lead to edema formation. Edema presents as a two- to three- fold increase in ear thickness within twenty-four hours.

The test compounds or standards can be applied (topical or parenteral) at various times before or after the sensitization or challenge phases. Increased ear thickness is prevented by several compounds including immunosuppressive agents and steroids. This model is a primary model for contact dermatitis.

(b) ALLOGENEIC SKIN TRANSPLANTATION

An allogeneic skin transplant model is used to identify immunosuppressive activity of test compounds. In this model, donor mouse thoracic skin (Balb/c) is surgically grafted onto the thorax of recipient mice (C57bl/6). Host rejection of the graft is evidenced by erythema, drying out, and retraction of donor skin. The mean graft survival time is 10 to 11 days, with 80% of the grafts being rejected by 12 days. Active novel immunosuppressive compounds, like existing immunosuppressive compounds, will prolong graft survival.

(c) POPLITEAL LYMPH NODE HYPERPLASIA

This model directly assesses T lymphocyte proliferation *in vivo*. Spleen cells, obtained from Balb/c mice, are isolated and administered into the foot pads of C3H mice. Within four days, the popliteal lymph nodes can be removed from the recipient mice and weighed. Other hematological assessments including FACS scanning for T lymphocyte subpopulations may also be performed. Active compounds, like existing immunosuppressive compounds, will inhibit the increase in node mass.

(d) RHEUMATOID ARTHRITIS

Several models are available for assessment of anti-arthritic activity, including adjuvant-induced, carageenan-induced, and collagen-induced arthritis in rats and/or mice. Paw pads are injected with one of these agents. Paws increase in volume, and measurements are made between 20 and 30 days later. The ability of test compounds to prevent the induction of paw swelling is tested with daily treatment for 12 consecutive days following the injection of inducing agent. The ability for the test compounds to reverse the progression of the paw swelling is tested by administration of the compound for 12 consecutive days beginning on the

twelfth day following the injection of inducing agent. Paw swelling measurements are made by water displacement plethysmography. Histology is also an appropriate endpoint for these studies. The MRL/lpr-mouse model, described above, is required for the rheumatoid arthritis indication. This model is a spontaneous autoimmune model that develops rheumatoid arthritis resembling the human condition, including the presence of circulating rheumatoid factor, pannus formation, and bone and cartilage erosion.

(e) SYSTEMIC LUPUS ERYTHEMATOSUS

Systemic lupus erythematosus is another autoimmune disease with several animal models. Several murine strains develop spontaneous SLE. One such strain is MRL/lpr-mice. These mice, over time (20 to 30 weeks) develop auto-antibodies against dsDNA, nuclear antigens, and renal basement membrane. This leads to complement fixation and immune complex formation. Damage to the kidney becomes apparent with the onset of proteinuria. Many of the other physiologic, hematologic, and immunologic aberrations described below for the CGVHD model are present. Immunosuppressive compounds such as cyclosporin, cyclophosphamide, and leflunomide can prevent and reverse the course of disease in this model. Interestingly, these mice also develop pathologies akin to rheumatoid arthritis.

The murine chronic graft versus host disease model (CGVHD, described below) is a model of SLE that contains many of the clinical features of SLE. Activity in this model has been shown to be predictive of activity in the more clinically relevant SLE models.

(f) TRANSPLANTATION

Allograft transplantation (skin graft) assay is often used as an initial test of immunosuppressive activity. While this model is useful as a screen, it may be supplemented with assays based on animal transplant models involving transplantation of internal organ (heart, liver, kidney, bone marrow) with use of "clinically acceptable" physiologic endpoints to assess graft survival. Efficacy of test compounds in only a very limited number of these rodent models is required. Following observation of activity in a rodent model, the test compounds are typically tested in further animal models (*e.g.*, canine, porcine or non-human primate). Active compounds decrease acute and chronic rejection and prolong transplant survival.

(g) GRAFT VS. HOST DISEASE

Chronic GVHD (CGVHD) can be used to model $CD4^+$-dependent humoral immunity. It is induced in BDF_1 mice (which are progeny of DBA/2 male x C57BL/6 female matings) by administering to them isolated spleen:lymph node cells from DBA/2 mice. This results in: a) disregulation and stimulation of $CD4^+$ T lymphocyte ($Ly1^+$; murine marker) activity due to incompatibilities at MHC II molecules, and b) abnormal T-B lymphocyte cooperation. The resulting pathological state, in many ways, mimics systemic lupus erythematosus (SLE). Several measurable endpoints develop within 14 days; including, circulating anti-host IgG and IgE antibodies, altered T and B lymphocyte proliferation activity measured *in vitro*, complement utilization, hemagglutination, slow progressive wasting, dermal aberrations, splenomegaly, lymphoid hyperplasia, and proteinuria. Only a few of these endpoints need to be measured.

Active compounds are are those which limit T lymphocyte disregulation and abrogate changes in these variables. Many steroids (*e.g.*, prednisolone), cyclosporine, FK-506, cyclophosphamide, and leflunomide are all active in this model and can be used as positive controls.

The acute GVHD model (AGVHD) is also produced in BDF_1 mice. In this case, isolated spleen:lymph node cells from C57BL/6 mice are administered. This results in disregulation and stimulation of $CD8^+$ T lymphocytes due to incompatibilities in the MHC I molecules. Elevated cytokine levels and donor clonal expansion occurs. Ultimately, donor cytotoxic T lymphocytes and NK cells rapidly reject host tissue and cause relatively rapid death of the recipient. The progression of AGVHD in this model is assessed by measurement of hematologic abnormalities (including T cell number and type), cytokine elevations (TNF, IL-1, IL-2, and/or IL-4), low body weight, hypoyglobulinemia, circulating hematologic characteristics indicative of aplastic anemia (granulocytopenia, thrombocytopenia), *ex vivo* NK or CTL activity, and host survival. Active compounds are those which abrogate changes in the variables, and prolong survival over 4 to 6 weeks.

(h) ASTHMA

Asthma offers another opportunity for safe immunosuppressive therapy. Atopic asthmatics have antibody mediated hypersensitivity and the often occurring late phase reaction is likened to a DTH response. Asthma has only recently been defined as an inflammatory disease (1992). Since then, several publications from prominent asthmatologists demonstrate the presence of activated $CD4^+$ and $CD8^+$ T lymphocytes in bronchoalveolar lavage fluid and blood of atopic asthmatics. The ratios of these cells changes in asthmatic conditions. Furthermore, several of the T cell associated cytokines (IL-1, IL-2, IL-4, IL-5, and TNF) are all implicated in clinical and experimental asthma. Inflammatory events in asthma are now considered to be T lymphocyte driven. Initial clinical trials with inhaled cyclosporin suggest that local immunosuppression can ameliorate airway hyperreactivity - the underlying defect in asthma.

The guinea pig model of antigen-induced pulmonary aberrations is used as a model for asthma. These animals are actively sensitized to ovalbumin to generate high circulating titers of anti-ovalbumin antibody with seroconversion to the IgE class, as is the case with atopic asthmatics. Aerosol challenge of sensitized guinea pigs results in measurable eosinophil rich pulmonary infiltrates (approximately a 16-fold increase in eosinophils), pulmonary edema, and mucous plugging of the small airways; all culminating in the expression of the underlying defect in asthma- airway hyperreactivity (approximately a 3 to 4-fold increase in reactivity). Acute bronchoconstriction is obviously present and points the aforementioned presence of the pathophysiologic sequelae. Active compounds are those which lessen or abrogate such symptoms.

The above description is meant to illustrate, rather than limit the scope of the invention. Given the foregoing description, numerous variations in the materials or methods employed in performing the invention will be obvious to one skilled in the art. Any such obvious variation is

to be considered within the scope of the invention. Full references to literature cited above (by reference to author and year) are provided below:

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Appendix I

ATOM	1	C	GLY	1	4.588	25.968	49.843	1.00	12.34	FKBP
ATOM	2	O	GLY	1	3.587	26.690	49.931	1.00	3.24	FKBP
ATOM	3	HT1	GLY	1	5.460	28.281	50.881	0.00	0.00	FKBP
ATOM	4	HT2	GLY	1	5.463	28.482	49.221	0.00	0.00	FKBP
ATOM	5	N	GLY	1	5.987	28.058	50.014	1.00	24.95	FKBP
ATOM	6	HT3	GLY	1	6.961	28.429	50.048	0.00	0.00	FKBP
ATOM	7	CA	GLY	1	5.986	26.568	49.849	1.00	14.30	FKBP
ATOM	8	N	VAL	2	4.539	24.648	49.684	1.00	9.85	FKBP
ATOM	9	H	VAL	2	5.366	24.143	49.539	0.00	0.00	FKBP
ATOM	10	CA	VAL	2	3.311	23.862	49.748	1.00	11.89	FKBP
ATOM	11	CB	VAL	2	2.889	23.360	48.318	1.00	9.17	FKBP
ATOM	12	CG1	VAL	2	4.114	23.006	47.492	1.00	14.93	FKBP
ATOM	13	CG2	VAL	2	1.975	22.155	48.411	1.00	2.00	FKBP
ATOM	14	C	VAL	2	3.549	22.668	50.692	1.00	15.67	FKBP
ATOM	15	O	VAL	2	4.576	21.989	50.605	1.00	16.61	FKBP
ATOM	16	N	GLN	3	2.643	22.482	51.646	1.00	17.91	FKBP
ATOM	17	H	GLN	3	1.852	23.045	51.649	0.00	0.00	FKBP
ATOM	18	CA	GLN	3	2.789	21.445	52.664	1.00	20.42	FKBP
ATOM	19	CB	GLN	3	2.600	22.065	54.056	1.00	26.51	FKBP
ATOM	20	CG	GLN	3	2.416	21.064	55.181	1.00	34.77	FKBP
ATOM	21	CD	GLN	3	3.718	20.451	55.660	1.00	41.28	FKBP
ATOM	22	OE1	GLN	3	4.754	20.581	55.015	1.00	44.41	FKBP
ATOM	23	NE2	GLN	3	3.665	19.760	56.792	1.00	42.31	FKBP
ATOM	24	HE21	GLN	3	2.812	19.651	57.241	0.00	0.00	FKBP
ATOM	25	HE22	GLN	3	4.510	19.373	57.085	0.00	0.00	FKBP
ATOM	26	C	GLN	3	1.817	20.280	52.454	1.00	17.06	FKBP
ATOM	27	O	GLN	3	0.608	20.466	52.367	1.00	17.79	FKBP
ATOM	28	N	VAL	4	2.363	19.082	52.313	1.00	14.50	FKBP
ATOM	29	H	VAL	4	3.336	19.008	52.381	0.00	0.00	FKBP
ATOM	30	CA	VAL	4	1.540	17.890	52.127	1.00	13.12	FKBP
ATOM	31	CB	VAL	4	2.054	17.030	50.930	1.00	10.68	FKBP
ATOM	32	CG1	VAL	4	0.924	16.172	50.364	1.00	7.51	FKBP
ATOM	33	CG2	VAL	4	2.630	17.930	49.842	1.00	9.85	FKBP
ATOM	34	C	VAL	4	1.544	17.037	53.401	1.00	12.15	FKBP
ATOM	35	O	VAL	4	2.600	16.705	53.947	1.00	15.65	FKBP
ATOM	36	N	GLU	5	0.363	16.733	53.914	1.00	6.97	FKBP
ATOM	37	H	GLU	5	-0.430	17.182	53.551	0.00	0.00	FKBP

	ATOM	38	CA	GLU	5	0.275	15.856	55.071	1.00	5.19	FKBP
	ATOM	39	CB	GLU	5	-0.096	16.664	56.308	1.00	8.81	FKBP
	ATOM	40	CG	GLU	5	0.621	17.998	56.389	1.00	13.30	FKBP
	ATOM	41	CD	GLU	5	0.346	18.726	57.674	1.00	15.76	FKBP
5	ATOM	42	OE1	GLU	5	1.188	18.629	58.586	1.00	22.97	FKBP
	ATOM	43	OE2	GLU	5	-0.710	19.385	57.778	1.00	22.20	FKBP
	ATOM	44	C	GLU	5	-0.743	14.752	54.848	1.00	3.46	FKBP
	ATOM	45	O	GLU	5	-1.937	15.023	54.745	1.00	4.04	FKBP
	ATOM	46	N	THR	6	-0.271	13.511	54.805	1.00	2.00	FKBP
10	ATOM	47	H	THR	6	0.666	13.372	55.050	0.00	0.00	FKBP
	ATOM	48	CA	THR	6	-1.125	12.365	54.508	1.00	5.26	FKBP
	ATOM	49	CB	THR	6	-0.337	11.045	54.575	1.00	3.67	FKBP
	ATOM	50	OG1	THR	6	0.881	11.178	53.836	1.00	13.50	FKBP
	ATOM	51	HG1	THR	6	1.493	10.508	54.158	0.00	0.00	FKBP
15	ATOM	52	CG2	THR	6	-1.132	9.919	53.972	1.00	2.01	FKBP
	ATOM	53	C	THR	6	-2.355	12.240	55.415	1.00	9.57	FKBP
	ATOM	54	O	THR	6	-2.281	12.454	56.629	1.00	15.36	FKBP
	ATOM	55	N	ILE	7	-3.509	12.099	54.772	1.00	8.03	FKBP
	ATOM	56	H	ILE	7	-3.506	12.334	53.824	0.00	0.00	FKBP
20	ATOM	57	CA	ILE	7	-4.755	11.709	55.423	1.00	7.62	FKBP
	ATOM	58	CB	ILE	7	-5.965	12.465	54.799	1.00	5.96	FKBP
	ATOM	59	CG2	ILE	7	-7.275	11.841	55.244	1.00	2.71	FKBP
	ATOM	60	CG1	ILE	7	-5.918	13.947	55.170	1.00	2.00	FKBP
	ATOM	61	CD1	ILE	7	-7.008	14.764	54.527	1.00	2.01	FKBP
25	ATOM	62	C	ILE	7	-4.979	10.199	55.249	1.00	11.96	FKBP
	ATOM	63	O	ILE	7	-5.686	9.576	56.034	1.00	17.57	FKBP
	ATOM	64	N	SER	8	-4.469	9.648	54.151	1.00	12.78	FKBP
	ATOM	65	H	SER	8	-4.039	10.240	53.499	0.00	0.00	FKBP
	ATOM	66	CA	SER	8	-4.629	8.226	53.842	1.00	12.24	FKBP
30	ATOM	67	CB	SER	8	-6.079	7.930	53.450	1.00	6.63	FKBP
	ATOM	68	OG	SER	8	-6.236	6.581	53.064	1.00	12.33	FKBP
	ATOM	69	HG	SER	8	-7.179	6.384	53.022	0.00	0.00	FKBP
	ATOM	70	C	SER	8	-3.685	7.798	52.707	1.00	19.11	FKBP
	ATOM	71	O	SER	8	-3.607	8.454	51.664	1.00	17.14	FKBP
35	ATOM	72	N	PRO	9	-2.830	6.798	52.965	1.00	23.27	FKBP
	ATOM	73	CD	PRO	9	-2.665	6.076	54.238	1.00	22.82	FKBP
	ATOM	74	CA	PRO	9	-1.706	6.548	52.055	1.00	25.68	FKBP
	ATOM	75	CB	PRO	9	-0.709	5.793	52.932	1.00	25.08	FKBP
	ATOM	76	CG	PRO	9	-1.572	5.093	53.920	1.00	26.18	FKBP

	ATOM	77	C	PRO	9	-2.056	5.766	50.778	1.00	28.63	FKBP
	ATOM	78	O	PRO	9	-3.034	5.014	50.737	1.00	30.17	FKBP
	ATOM	79	N	GLY	10	-1.272	5.988	49.728	1.00	28.78	FKBP
	ATOM	80	H	GLY	10	-0.602	6.696	49.796	0.00	0.00	FKBP
5	ATOM	81	CA	GLY	10	-1.373	5.168	48.531	1.00	32.81	FKBP
	ATOM	82	C	GLY	10	-0.241	4.154	48.412	1.00	34.72	FKBP
	ATOM	83	O	GLY	10	0.479	3.916	49.386	1.00	37.49	FKBP
	ATOM	84	N	ASP	11	-0.018	3.626	47.208	1.00	30.71	FKBP
	ATOM	85	H	ASP	11	-0.664	3.846	46.504	0.00	0.00	FKBP
10	ATOM	86	CA	ASP	11	0.992	2.585	47.006	1.00	28.23	FKBP
	ATOM	87	CB	ASP	11	0.767	1.862	45.675	1.00	23.26	FKBP
	ATOM	88	CG	ASP	11	0.713	2.804	44.493	1.00	21.83	FKBP
	ATOM	89	OD1	ASP	11	1.591	3.686	44.377	1.00	13.66	FKBP
	ATOM	90	OD2	ASP	11	-0.204	2.635	43.659	1.00	23.38	FKBP
15	ATOM	91	C	ASP	11	2.438	3.073	47.085	1.00	29.86	FKBP
	ATOM	92	O	ASP	11	3.364	2.273	47.190	1.00	31.65	FKBP
	ATOM	93	N	GLY	12	2.637	4.372	46.898	1.00	31.53	FKBP
	ATOM	94	H	GLY	12	1.858	4.932	46.696	0.00	0.00	FKBP
	ATOM	95	CA	GLY	12	3.958	4.948	47.081	1.00	34.79	FKBP
20	ATOM	96	C	GLY	12	4.976	4.585	46.015	1.00	37.89	FKBP
	ATOM	97	O	GLY	12	6.183	4.621	46.262	1.00	38.20	FKBP
	ATOM	98	N	ARG	13	4.488	4.222	44.833	1.00	40.35	FKBP
	ATOM	99	H	ARG	13	3.572	3.918	44.840	0.00	0.00	FKBP
	ATOM	100	CA	ARG	13	5.357	4.030	43.667	1.00	43.98	FKBP
25	ATOM	101	CB	ARG	13	5.756	2.552	43.526	1.00	48.12	FKBP
	ATOM	102	CG	ARG	13	4.624	1.555	43.724	1.00	56.08	FKBP
	ATOM	103	CD	ARG	13	5.130	0.296	44.418	1.00	64.50	FKBP
	ATOM	104	NE	ARG	13	4.963	0.361	45.870	1.00	70.55	FKBP
	ATOM	105	HE	ARG	13	5.508	1.005	46.370	0.00	0.00	FKBP
30	ATOM	106	CZ	ARG	13	4.154	-0.435	46.567	1.00	73.54	FKBP
	ATOM	107	NH1	ARG	13	4.023	-0.266	47.877	1.00	74.82	FKBP
	ATOM	108	HH11	ARG	13	4.540	0.450	48.341	0.00	0.00	FKBP
	ATOM	109	HH12	ARG	13	3.414	-0.864	48.399	0.00	0.00	FKBP
	ATOM	110	NH2	ARG	13	3.490	-1.415	45.961	1.00	75.14	FKBP
35	ATOM	111	HH21	ARG	13	3.595	-1.557	44.977	0.00	0.00	FKBP
	ATOM	112	HH22	ARG	13	2.873	-2.001	46.485	0.00	0.00	FKBP
	ATOM	113	C	ARG	13	4.720	4.537	42.369	1.00	40.88	FKBP
	ATOM	114	O	ARG	13	5.414	4.995	41.459	1.00	41.05	FKBP
	ATOM	115	N	THR	14	3.392	4.531	42.328	1.00	36.51	FKBP

ATOM	116	H	THR	14	2.944	3.906	42.915	0.00	0.00	FKBP
ATOM	117	CA	THR	14	2.654	5.085	41.199	1.00	31.82	FKBP
ATOM	118	CB	THR	14	1.296	4.362	41.010	1.00	34.22	FKBP
ATOM	119	OG1	THR	14	1.477	2.945	41.172	1.00	31.38	FKBP
ATOM	120	HG1	THR	14	0.659	2.484	40.952	0.00	0.00	FKBP
ATOM	121	CG2	THR	14	0.722	4.651	39.621	1.00	29.70	FKBP
ATOM	122	C	THR	14	2.416	6.589	41.356	1.00	28.19	FKBP
ATOM	123	O	THR	14	1.373	7.023	41.846	1.00	25.30	FKBP
ATOM	124	N	PHE	15	3.430	7.364	41.000	1.00	27.12	FKBP
ATOM	125	H	PHE	15	4.257	6.922	40.707	0.00	0.00	FKBP
ATOM	126	CA	PHE	15	3.354	8.822	40.970	1.00	30.73	FKBP
ATOM	127	CB	PHE	15	4.725	9.405	41.330	1.00	30.56	FKBP
ATOM	128	CG	PHE	15	5.202	9.018	42.701	1.00	31.81	FKBP
ATOM	129	CD1	PHE	15	5.046	9.885	43.775	1.00	31.26	FKBP
ATOM	130	CD2	PHE	15	5.732	7.756	42.936	1.00	31.84	FKBP
ATOM	131	CE1	PHE	15	5.400	9.499	45.062	1.00	28.40	FKBP
ATOM	132	CE2	PHE	15	6.089	7.363	44.218	1.00	31.05	FKBP
ATOM	133	CZ	PHE	15	5.919	8.237	45.283	1.00	31.16	FKBP
ATOM	134	C	PHE	15	2.902	9.358	39.596	1.00	34.59	FKBP
ATOM	135	O	PHE	15	3.176	8.739	38.557	1.00	32.29	FKBP
ATOM	136	N	PRO	16	2.232	10.532	39.571	1.00	35.21	FKBP
ATOM	137	CD	PRO	16	2.068	11.493	40.671	1.00	32.43	FKBP
ATOM	138	CA	PRO	16	1.814	11.122	38.296	1.00	36.14	FKBP
ATOM	139	CB	PRO	16	0.852	12.243	38.710	1.00	33.90	FKBP
ATOM	140	CG	PRO	16	0.905	12.310	40.215	1.00	34.16	FKBP
ATOM	141	C	PRO	16	2.998	11.672	37.512	1.00	38.59	FKBP
ATOM	142	O	PRO	16	3.580	12.683	37.895	1.00	40.62	FKBP
ATOM	143	N	LYS	17	3.408	10.958	36.467	1.00	44.97	FKBP
ATOM	144	H	LYS	17	3.044	10.054	36.366	0.00	0.00	FKBP
ATOM	145	CA	LYS	17	4.463	11.441	35.572	1.00	49.95	FKBP
ATOM	146	CB	LYS	17	4.856	10.356	34.563	1.00	53.22	FKBP
ATOM	147	CG	LYS	17	5.973	9.427	35.030	1.00	61.47	FKBP
ATOM	148	CD	LYS	17	5.425	8.075	35.497	1.00	69.15	FKBP
ATOM	149	CE	LYS	17	6.545	7.050	35.721	1.00	73.13	FKBP
ATOM	150	NZ	LYS	17	6.050	5.706	36.174	1.00	72.77	FKBP
ATOM	151	HZ1	LYS	17	5.395	5.316	35.466	0.00	0.00	FKBP
ATOM	152	HZ2	LYS	17	5.550	5.803	37.081	0.00	0.00	FKBP
ATOM	153	HZ3	LYS	17	6.857	5.061	36.292	0.00	0.00	FKBP
ATOM	154	C	LYS	17	4.031	12.703	34.823	1.00	50.23	FKBP

	ATOM	155	O	LYS	17	2.882	12.813	34.389	1.00	51.36	FKBP
	ATOM	156	N	ARG	18	4.938	13.672	34.718	1.00	48.43	FKBP
	ATOM	157	H	ARG	18	5.782	13.553	35.190	0.00	0.00	FKBP
	ATOM	158	CA	ARG	18	4.666	14.908	33.986	1.00	46.13	FKBP
5	ATOM	159	CB	ARG	18	5.968	15.671	33.732	1.00	47.22	FKBP
	ATOM	160	CG	ARG	18	5.755	17.034	33.092	1.00	53.52	FKBP
	ATOM	161	CD	ARG	18	7.030	17.572	32.467	1.00	60.93	FKBP
	ATOM	162	NE	ARG	18	8.005	18.008	33.466	1.00	68.56	FKBP
	ATOM	163	HE	ARG	18	8.698	17.375	33.748	0.00	0.00	FKBP
10	ATOM	164	CZ	ARG	18	7.995	19.201	34.054	1.00	71.82	FKBP
	ATOM	165	NH1	ARG	18	8.954	19.528	34.910	1.00	73.41	FKBP
	ATOM	166	HH11	ARG	18	9.674	18.876	35.143	0.00	0.00	FKBP
	ATOM	167	HH12	ARG	18	8.923	20.425	35.358	0.00	0.00	FKBP
	ATOM	168	NH2	ARG	18	7.000	20.052	33.826	1.00	74.07	FKBP
15	ATOM	169	HH21	ARG	18	6.256	19.798	33.207	0.00	0.00	FKBP
	ATOM	170	HH22	ARG	18	6.994	20.950	34.267	0.00	0.00	FKBP
	ATOM	171	C	ARG	18	3.965	14.637	32.652	1.00	44.43	FKBP
	ATOM	172	O	ARG	18	4.440	13.832	31.844	1.00	44.85	FKBP
	ATOM	173	N	GLY	19	2.775	15.209	32.491	1.00	41.63	FKBP
20	ATOM	174	H	GLY	19	2.437	15.781	33.210	0.00	0.00	FKBP
	ATOM	175	CA	GLY	19	2.037	15.058	31.246	1.00	36.64	FKBP
	ATOM	176	C	GLY	19	0.878	14.072	31.281	1.00	33.71	FKBP
	ATOM	177	O	GLY	19	0.242	13.821	30.256	1.00	31.30	FKBP
	ATOM	178	N	GLN	20	0.603	13.509	32.454	1.00	31.51	FKBP
25	ATOM	179	H	GLN	20	1.278	13.579	33.162	0.00	0.00	FKBP
	ATOM	180	CA	GLN	20	-0.571	12.655	32.647	1.00	27.89	FKBP
	ATOM	181	CB	GLN	20	-0.290	11.586	33.702	1.00	27.47	FKBP
	ATOM	182	CG	GLN	20	0.907	10.723	33.416	1.00	29.05	FKBP
	ATOM	183	CD	GLN	20	0.945	9.516	34.305	1.00	28.73	FKBP
30	ATOM	184	OE1	GLN	20	1.852	9.355	35.112	1.00	29.95	FKBP
	ATOM	185	NE2	GLN	20	-0.064	8.672	34.191	1.00	29.76	FKBP
	ATOM	186	HE21	GLN	20	-0.781	8.854	33.542	0.00	0.00	FKBP
	ATOM	187	HE22	GLN	20	-0.025	7.895	34.776	0.00	0.00	FKBP
	ATOM	188	C	GLN	20	-1.784	13.458	33.096	1.00	26.36	FKBP
35	ATOM	189	O	GLN	20	-1.641	14.558	33.652	1.00	23.69	FKBP
	ATOM	190	N	THR	21	-2.957	12.836	32.994	1.00	23.74	FKBP
	ATOM	191	H	THR	21	-2.993	11.964	32.525	0.00	0.00	FKBP
	ATOM	192	CA	THR	21	-4.185	13.406	33.551	1.00	19.78	FKBP
	ATOM	193	CB	THR	21	-5.398	13..137	32.648	1.00	18.09	FKBP

ATOM	194	OG1	THR	21	-5.103	13.576	31.319	1.00	25.65	FKBP
ATOM	195	HG1	THR	21	-4.667	12.831	30.862	0.00	0.00	FKBP
ATOM	196	CG2	THR	21	-6.624	13.882	33.159	1.00	15.30	FKBP
ATOM	197	C	THR	21	-4.502	12.869	34.945	1.00	19.51	FKBP
ATOM	198	O	THR	21	-4.895	11.707	35.112	1.00	21.36	FKBP
ATOM	199	N	CYS	22	-4.390	13.744	35.939	1.00	15.33	FKBP
ATOM	200	H	CYS	22	-4.044	14.636	35.726	0.00	0.00	FKBP
ATOM	201	CA	CYS	22	-4.794	13.421	37.302	1.00	7.92	FKBP
ATOM	202	CB	CYS	22	-4.056	14.322	38.281	1.00	4.88	FKBP
ATOM	203	SG	CYS	22	-2.300	14.464	37.959	1.00	9.58	FKBP
ATOM	204	C	CYS	22	-6.301	13.589	37.492	1.00	7.02	FKBP
ATOM	205	O	CYS	22	-6.840	14.676	37.284	1.00	8.66	FKBP
ATOM	206	N	VAL	23	-6.991	12.485	37.760	1.00	4.33	FKBP
ATOM	207	H	VAL	23	-6.547	11.617	37.634	0.00	0.00	FKBP
ATOM	208	CA	VAL	23	-8.371	12.542	38.232	1.00	6.31	FKBP
ATOM	209	CB	VAL	23	-9.180	11.314	37.743	1.00	3.87	FKBP
ATOM	210	CG1	VAL	23	-10.658	11.483	38.043	1.00	2.00	FKBP
ATOM	211	CG2	VAL	23	-8.972	11.121	36.264	1.00	5.84	FKBP
ATOM	212	C	VAL	23	-8.353	12.579	39.770	1.00	11.82	FKBP
ATOM	213	O	VAL	23	-7.678	11.765	40.416	1.00	17.38	FKBP
ATOM	214	N	VAL	24	-8.946	13.622	40.342	1.00	10.13	FKBP
ATOM	215	H	VAL	24	-9.395	14.274	39.762	0.00	0.00	FKBP
ATOM	216	CA	VAL	24	-8.896	13.840	41.782	1.00	5.89	FKBP
ATOM	217	CB	VAL	24	-7.806	14.883	42.170	1.00	3.59	FKBP
ATOM	218	CG1	VAL	24	-6.481	14.535	41.524	1.00	2.00	FKBP
ATOM	219	CG2	VAL	24	-8.238	16.276	41.784	1.00	2.66	FKBP
ATOM	220	C	VAL	24	-10.237	14.309	42.333	1.00	7.13	FKBP
ATOM	221	O	VAL	24	-11.078	14.804	41.583	1.00	8.15	FKBP
ATOM	222	N	HIS	25	-10.481	14.041	43.617	1.00	8.15	FKBP
ATOM	223	H	HIS	25	-9.837	13.454	44.074	0.00	0.00	FKBP
ATOM	224	CA	HIS	25	-11.588	14.671	44.346	1.00	5.84	FKBP
ATOM	225	CB	HIS	25	-12.462	13.611	45.015	1.00	2.00	FKBP
ATOM	226	CG	HIS	25	-13.789	13.412	44.351	1.00	2.00	FKBP
ATOM	227	CD2	HIS	25	-14.625	12.348	44.335	1.00	2.01	FKBP
ATOM	228	ND1	HIS	25	-14.420	14.398	43.625	1.00	6.75	FKBP
ATOM	229	HD1	HIS	25	-13.990	15.194	43.216	0.00	0.00	FKBP
ATOM	230	CE1	HIS	25	-15.591	13.959	43.204	1.00	2.00	FKBP
ATOM	231	NE2	HIS	25	-15.738	12.715	43.619	1.00	2.00	FKBP
ATOM	232	HE2	HIS	25	-16.532	12.146	43.449	0.00	0.00	FKBP

ATOM	233	C	HIS	25	-11.013	15.611	45.409	1.00	5.86	FKBP
ATOM	234	O	HIS	25	-10.085	15.233	46.125	1.00	8.08	FKBP
ATOM	235	N	TYR	26	-11.456	16.867	45.414	1.00	2.00	FKBP
ATOM	236	H	TYR	26	-12.071	17.155	44.712	0.00	0.00	FKBP
ATOM	237	CA	TYR	26	-10.956	17.840	46.389	1.00	2.00	FKBP
ATOM	238	CB	TYR	26	-9.950	18.827	45.770	1.00	3.39	FKBP
ATOM	239	CG	TYR	26	-10.570	19.839	44.824	1.00	8.68	FKBP
ATOM	240	CD1	TYR	26	-11.017	21.080	45.279	1.00	7.15	FKBP
ATOM	241	CE1	TYR	26	-11.725	21.939	44.434	1.00	11.31	FKBP
ATOM	242	CD2	TYR	26	-10.831	19.497	43.495	1.00	11.88	FKBP
ATOM	243	CE2	TYR	26	-11.536	20.342	42.651	1.00	8.71	FKBP
ATOM	244	CZ	TYR	26	-11.982	21.551	43.122	1.00	9.36	FKBP
ATOM	245	OH	TYR	26	-12.704	22.348	42.274	1.00	9.02	FKBP
ATOM	246	HH	TYR	26	-12.792	21.935	41.411	0.00	0.00	FKBP
ATOM	247	C	TYR	26	-12.057	18.638	47.045	1.00	2.60	FKBP
ATOM	248	O	TYR	26	-13.162	18.746	46.515	1.00	2.96	FKBP
ATOM	249	N	THR	27	-11.778	19.056	48.276	1.00	8.98	FKBP
ATOM	250	H	THR	27	-11.030	18.611	48.735	0.00	0.00	FKBP
ATOM	251	CA	THR	27	-12.469	20.164	48.924	1.00	3.70	FKBP
ATOM	252	CB	THR	27	-13.138	19.737	50.219	1.00	3.82	FKBP
ATOM	253	OG1	THR	27	-13.987	18.606	49.972	1.00	5.37	FKBP
ATOM	254	HG1	THR	27	-13.409	17.851	49.785	0.00	0.00	FKBP
ATOM	255	CG2	THR	27	-13.957	20.891	50.779	1.00	2.73	FKBP
ATOM	256	C	THR	27	-11.436	21.213	49.273	1.00	2.00	FKBP
ATOM	257	O	THR	27	-10.365	20.891	49.784	1.00	2.00	FKBP
ATOM	258	N	GLY	28	-11.664	22.419	48.779	1.00	5.64	FKBP
ATOM	259	H	GLY	28	-12.274	22.498	48.038	0.00	0.00	FKBP
ATOM	260	CA	GLY	28	-10.813	23.538	49.128	1.00	8.04	FKBP
ATOM	261	C	GLY	28	-11.438	24.437	50.175	1.00	8.15	FKBP
ATOM	262	O	GLY	28	-12.646	24.729	50.131	1.00	9.73	FKBP
ATOM	263	N	MET	29	-10.619	24.887	51.117	1.00	4.38	FKBP
ATOM	264	H	MET	29	-9.683	24.601	51.122	0.00	0.00	FKBP
ATOM	265	CA	MET	29	-11.091	25.812	52.138	1.00	6.14	FKBP
ATOM	266	CB	MET	29	-11.512	25.047	53.404	1.00	11.72	FKBP
ATOM	267	CG	MET	29	-10.445	24.128	53.999	1.00	14.88	FKBP
ATOM	268	SD	MET	29	-11.065	22.500	54.510	1.00	7.90	FKBP
ATOM	269	CE	MET	29	-12.824	22.854	54.721	1.00	5.60	FKBP
ATOM	270	C	MET	29	-10.033	26.845	52.477	1.00	6.50	FKBP
ATOM	271	O	MET	29	-8.847	26.630	52.242	1.00	5.89	FKBP

ATOM	272	N	LEU	30	-10.477	28.013	52.923	1.00	11.28	FKBP
ATOM	273	H	LEU	30	-11.444	28.168	52.902	0.00	0.00	FKBP
ATOM	274	CA	LEU	30	-9.561	29.028	53.443	1.00	14.74	FKBP
ATOM	275	CB	LEU	30	-10.281	30.379	53.572	1.00	12.99	FKBP
ATOM	276	CG	LEU	30	-10.887	30.967	52.292	1.00	10.36	FKBP
ATOM	277	CD1	LEU	30	-12.064	31.842	52.668	1.00	12.99	FKBP
ATOM	278	CD2	LEU	30	-9.848	31.761	51.510	1.00	3.34	FKBP
ATOM	279	C	LEU	30	-9.042	28.573	54.805	1.00	14.12	FKBP
ATOM	280	O	LEU	30	-9.664	27.732	55.453	1.00	16.16	FKBP
ATOM	281	N	GLU	31	-7.944	29.169	55.262	1.00	14.66	FKBP
ATOM	282	H	GLU	31	-7.506	29.828	54.682	0.00	0.00	FKBP
ATOM	283	CA	GLU	31	-7.266	28.722	56.483	1.00	17.28	FKBP
ATOM	284	CB	GLU	31	-6.294	29.799	56.962	1.00	14.61	FKBP
ATOM	285	CG	GLU	31	-5.818	29.586	58.382	1.00	22.25	FKBP
ATOM	286	CD	GLU	31	-4.510	30.284	58.698	1.00	26.77	FKBP
ATOM	287	OE1	GLU	31	-4.245	31.362	58.107	1.00	21.74	FKBP
ATOM	288	OE2	GLU	31	-3.774	29.762	59.576	1.00	23.08	FKBP
ATOM	289	C	GLU	31	-8.187	28.313	57.642	1.00	18.96	FKBP
ATOM	290	O	GLU	31	-8.008	27.258	58.262	1.00	18.93	FKBP
ATOM	291	N	ASP	32	-9.238	29.090	57.855	1.00	17.34	FKBP
ATOM	292	H	ASP	32	-9.405	29.814	57.223	0.00	0.00	FKBP
ATOM	293	CA	ASP	32	-10.116	28.866	58.996	1.00	19.84	FKBP
ATOM	294	CB	ASP	32	-10.894	30.142	59.308	1.00	27.98	FKBP
ATOM	295	CG	ASP	32	-11.601	30.704	58.090	1.00	34.72	FKBP
ATOM	296	OD1	ASP	32	-12.727	30.254	57.801	1.00	32.49	FKBP
ATOM	297	OD2	ASP	32	-11.023	31.588	57.415	1.00	43.34	FKBP
ATOM	298	C	ASP	32	-11.096	27.713	58.816	1.00	18.08	FKBP
ATOM	299	O	ASP	32	-11.986	27.541	59.638	1.00	17.85	FKBP
ATOM	300	N	GLY	33	-10.994	26.998	57.697	1.00	18.90	FKBP
ATOM	301	H	GLY	33	-10.204	27.111	57.137	0.00	0.00	FKBP
ATOM	302	CA	GLY	33	-11.909	25.896	57.417	1.00	14.65	FKBP
ATOM	303	C	GLY	33	-13.146	26.270	56.616	1.00	10.95	FKBP
ATOM	304	O	GLY	33	-14.020	25.437	56.370	1.00	11.28	FKBP
ATOM	305	N	LYS	34	-13.235	27.536	56.230	1.00	5.53	FKBP
ATOM	306	H	LYS	34	-12.565	28.159	56.564	0.00	0.00	FKBP
ATOM	307	CA	LYS	34	-14.320	27.999	55.379	1.00	7.65	FKBP
ATOM	308	CB	LYS	34	-14.270	29.521	55.255	1.00	15.91	FKBP
ATOM	309	CG	LYS	34	-15.468	30.131	54.554	1.00	23.47	FKBP
ATOM	310	CD	LYS	34	-15.360	31.646	54.513	1.00	34.71	FKBP

	ATOM	311	CE	LYS	34	-15.213	32.245	55.918	1.00	38.38	FKBP
	ATOM	312	NZ	LYS	34	-13.805	32.635	56.227	1.00	41.83	FKBP
	ATOM	313	HZ1	LYS	34	-13.475	33.324	55.520	0.00	0.00	FKBP
	ATOM	314	HZ2	LYS	34	-13.196	31.792	56.185	0.00	0.00	FKBP
	ATOM	315	HZ3	LYS	34	-13.749	33.055	57.176	0.00	0.00	FKBP
	ATOM	316	C	LYS	34	-14.222	27.369	53.991	1.00	7.56	FKBP
	ATOM	317	O	LYS	34	-13.290	27.653	53.232	1.00	3.26	FKBP
	ATOM	318	N	LYS	35	-15.067	26.371	53.757	1.00	8.73	FKBP
	ATOM	319	H	LYS	35	-15.554	26.012	54.530	0.00	0.00	FKBP
	ATOM	320	CA	LYS	35	-15.178	25.719	52.459	1.00	8.15	FKBP
	ATOM	321	CB	LYS	35	-16.269	24.657	52.511	1.00	2.40	FKBP
	ATOM	322	CG	LYS	35	-16.379	23.854	51.249	1.00	7.41	FKBP
	ATOM	323	CD	LYS	35	-17.142	22.573	51.484	1.00	11.33	FKBP
	ATOM	324	CE	LYS	35	-18.637	22.803	51.464	1.00	15.67	FKBP
	ATOM	325	NZ	LYS	35	-19.352	21.501	51.304	1.00	20.77	FKBP
	ATOM	326	HZ1	LYS	35	-19.180	20.892	52.129	0.00	0.00	FKBP
	ATOM	327	HZ2	LYS	35	-19.004	21.025	50.450	0.00	0.00	FKBP
	ATOM	328	HZ3	LYS	35	-20.373	21.681	51.212	0.00	0.00	FKBP
	ATOM	329	C	LYS	35	-15.520	26.736	51.378	1.00	13.32	FKBP
	ATOM	330	O	LYS	35	-16.387	27.596	51.587	1.00	16.59	FKBP
	ATOM	331	N	PHE	36	-14.796	26.690	50.257	1.00	12.19	FKBP
	ATOM	332	H	PHE	36	-13.981	26.149	50.278	0.00	0.00	FKBP
	ATOM	333	CA	PHE	36	-15.167	27.504	49.098	1.00	8.93	FKBP
	ATOM	334	CB	PHE	36	-14.077	28.541	48.753	1.00	4.86	FKBP
	ATOM	335	CG	PHE	36	-12.728	27.959	48.415	1.00	3.36	FKBP
	ATOM	336	CD1	PHE	36	-11.660	28.108	49.295	1.00	4.33	FKBP
	ATOM	337	CD2	PHE	36	-12.470	27.442	47.151	1.00	7.57	FKBP
	ATOM	338	CE1	PHE	36	-10.350	27.758	48.916	1.00	5.11	FKBP
	ATOM	339	CE2	PHE	36	-11.167	27.092	46.766	1.00	5.95	FKBP
	ATOM	340	CZ	PHE	36	-10.110	27.250	47.648	1.00	2.00	FKBP
	ATOM	341	C	PHE	36	-15.553	26.696	47.861	1.00	11.24	FKBP
	ATOM	342	O	PHE	36	-16.499	27.050	47.152	1.00	9.15	FKBP
	ATOM	343	N	ASP	37	-14.972	25.507	47.738	1.00	11.21	FKBP
	ATOM	344	H	ASP	37	-14.365	25.202	48.445	0.00	0.00	FKBP
	ATOM	345	CA	ASP	37	-15.201	24.672	46.568	1.00	8.81	FKBP
	ATOM	346	CB	ASP	37	-14.340	25.220	45.416	1.00	12.70	FKBP
	ATOM	347	CG	ASP	37	-14.583	24.518	44.091	1.00	11.57	FKBP
	ATOM	348	OD1	ASP	37	-15.679	23.968	43.855	1.00	7.88	FKBP
	ATOM	349	OD2	ASP	37	-13.665	24.565	43.254	1.00	15.66	FKBP

	ATOM	350	C	ASP	37	-14.874	23.199	46.864	1.00	2.00	FKBP
	ATOM	351	O	ASP	37	-13.905	22.904	47.545	1.00	2.01	FKBP
	ATOM	352	N	SER	38	-15.751	22.291	46.450	1.00	2.52	FKBP
	ATOM	353	H	SER	38	-16.607	22.613	46.095	0.00	0.00	FKBP
5	ATOM	354	CA	SER	38	-15.461	20.850	46.493	1.00	2.33	FKBP
	ATOM	355	CB	SER	38	-15.954	20.223	47.800	1.00	12.19	FKBP
	ATOM	356	OG	SER	38	-15.979	18.804	47.722	1.00	9.54	FKBP
	ATOM	357	HG	SER	38	-15.613	18.490	48.571	0.00	0.00	FKBP
	ATOM	358	C	SER	38	-16.108	20.110	45.349	1.00	2.00	FKBP
10	ATOM	359	O	SER	38	-17.313	20.210	45.168	1.00	2.31	FKBP
	ATOM	360	N	SER	39	-15.339	19.252	44.684	1.00	2.00	FKBP
	ATOM	361	H	SER	39	-14.397	19.223	44.967	0.00	0.00	FKBP
	ATOM	362	CA	SER	39	-15.840	18.414	43.584	1.00	3.72	FKBP
	ATOM	363	CB	SER	39	-14.682	17.758	42.825	1.00	3.50	FKBP
15	ATOM	364	OG	SER	39	-13.861	16.976	43.683	1.00	3.28	FKBP
	ATOM	365	HG	SER	39	-14.195	17.054	44.589	0.00	0.00	FKBP
	ATOM	366	C	SER	39	-16.762	17.317	44.088	1.00	9.63	FKBP
	ATOM	367	O	SER	39	-17.547	16.751	43.324	1.00	6.74	FKBP
	ATOM	368	N	ARG	40	-16.624	16.994	45.376	1.00	13.48	FKBP
20	ATOM	369	H	ARG	40	-16.027	17.536	45.944	0.00	0.00	FKBP
	ATOM	370	CA	ARG	40	-17.441	15.972	46.025	1.00	12.15	FKBP
	ATOM	371	CB	ARG	40	-16.800	15.538	47.345	1.00	4.43	FKBP
	ATOM	372	CG	ARG	40	-15.385	15.003	47.220	1.00	2.00	FKBP
	ATOM	373	CD	ARG	40	-14.978	14.243	48.484	1.00	3.29	FKBP
25	ATOM	374	NE	ARG	40	-13.546	13.940	48.561	1.00	4.66	FKBP
	ATOM	375	HE	ARG	40	-12.924	14.683	48.660	0.00	0.00	FKBP
	ATOM	376	CZ	ARG	40	-13.031	12.714	48.497	1.00	2.00	FKBP
	ATOM	377	NH1	ARG	40	-11.727	12.527	48.631	1.00	2.00	FKBP
	ATOM	378	HH11	ARG	40	-11.112	13.308	48.782	0.00	0.00	FKBP
30	ATOM	379	HH12	ARG	40	-11.374	11.597	48.585	0.00	0.00	FKBP
	ATOM	380	NH2	ARG	40	-13.812	11.673	48.262	1.00	2.00	FKBP
	ATOM	381	HH21	ARG	40	-14.794	11.785	48.128	0.00	0.00	FKBP
	ATOM	382	HH22	ARG	40	-13.417	10.752	48.214	0.00	0.00	FKBP
	ATOM	383	C	ARG	40	-18.883	16.433	46.270	1.00	17.11	FKBP
35	ATOM	384	O	ARG	40	-19.798	15.612	46.350	1.00	17.06	FKBP
	ATOM	385	N	ASP	41	-19.085	17.746	46.370	1.00	20.79	FKBP
	ATOM	386	H	ASP	41	-18.307	18.340	46.438	0.00	0.00	FKBP
	ATOM	387	CA	ASP	41	-20.435	18.315	46.454	1.00	26.68	FKBP
	ATOM	388	CB	ASP	41	-20.375	19.784	46.879	1.00	26.55	FKBP

	ATOM	389	CG	ASP	41	-19.641	19.993	48.195	1.00	34.97	FKBP
	ATOM	390	OD1	ASP	41	-19.251	19.001	48.852	1.00	38.14	FKBP
	ATOM	391	OD2	ASP	41	-19.426	21.167	48.559	1.00	36.52	FKBP
	ATOM	392	C	ASP	41	-21.187	18.206	45.124	1.00	30.48	FKBP
5	ATOM	393	O	ASP	41	-22.416	18.085	45.106	1.00	31.53	FKBP
	ATOM	394	N	ARG	42	-20.447	18.307	44.018	1.00	31.99	FKBP
	ATOM	395	H	ARG	42	-19.519	18.595	44.120	0.00	0.00	FKBP
	ATOM	396	CA	ARG	42	-21.006	18.124	42.676	1.00	26.25	FKBP
	ATOM	397	CB	ARG	42	-20.168	18.865	41.625	1.00	22.17	FKBP
10	ATOM	398	CG	ARG	42	-19.815	20.302	41.976	1.00	26.16	FKBP
	ATOM	399	CD	ARG	42	-18.697	20.840	41.089	1.00	29.95	FKBP
	ATOM	400	NE	ARG	42	-17.703	19.814	40.769	1.00	40.62	FKBP
	ATOM	401	HE	ARG	42	-17.911	18.869	40.922	0.00	0.00	FKBP
	ATOM	402	CZ	ARG	42	-16.491	20.058	40.273	1.00	44.80	FKBP
15	ATOM	403	NH1	ARG	42	-15.684	19.045	39.978	1.00	43.55	FKBP
	ATOM	404	HH11	ARG	42	-16.002	18.108	40.125	0.00	0.00	FKBP
	ATOM	405	HH12	ARG	42	-14.773	19.213	39.600	0.00	0.00	FKBP
	ATOM	406	NH2	ARG	42	-16.070	21.306	40.089	1.00	47.04	FKBP
	ATOM	407	HH21	ARG	42	-16.655	22.080	40.328	0.00	0.00	FKBP
20	ATOM	408	HH22	ARG	42	-15.156	21.465	39.719	0.00	0.00	FKBP
	ATOM	409	C	ARG	42	-21.051	16.642	42.320	1.00	25.62	FKBP
	ATOM	410	O	ARG	42	-21.679	16.252	41.338	1.00	29.04	FKBP
	ATOM	411	N	ASN	43	-20.302	15.832	43.064	1.00	20.94	FKBP
	ATOM	412	H	ASN	43	-19.786	16.217	43.793	0.00	0.00	FKBP
25	ATOM	413	CA	ASN	43	-20.290	14.392	42.840	1.00	21.52	FKBP
	ATOM	414	CB	ASN	43	-21.724	13.852	42.869	1.00	23.52	FKBP
	ATOM	415	CG	ASN	43	-21.808	12.455	43.431	1.00	28.90	FKBP
	ATOM	416	OD1	ASN	43	-20.789	11.802	43.662	1.00	28.67	FKBP
	ATOM	417	ND2	ASN	43	-23.025	11.987	43.662	1.00	33.33	FKBP
30	ATOM	418	HD21	ASN	43	-23.786	12.557	43.466	0.00	0.00	FKBP
	ATOM	419	HD22	ASN	43	-23.041	11.094	44.043	0.00	0.00	FKBP
	ATOM	420	C	ASN	43	-19.628	14.078	41.498	1.00	20.93	FKBP
	ATOM	421	O	ASN	43	-20.087	13.228	40.740	1.00	21.51	FKBP
	ATOM	422	N	LYS	44	-18.475	14.696	41.275	1.00	20.83	FKBP
35	ATOM	423	H	LYS	44	-18.152	15.288	41.984	0.00	0.00	FKBP
	ATOM	424	CA	LYS	44	-17.874	14.757	39.947	1.00	19.75	FKBP
	ATOM	425	CB	LYS	44	-18.554	15.879	39.148	1.00	24.43	FKBP
	ATOM	426	CG	LYS	44	-18.478	15.755	37.638	1.00	23.61	FKBP
	ATOM	427	CD	LYS	44	-18.796	17.084	36.965	1.00	29.64	FKBP

ATOM	428	CE	LYS	44	-20.212	17.565	37.282	1.00	34.29	FKBP
ATOM	429	NZ	LYS	44	-20.543	18.848	36.583	1.00	38.07	FKBP
ATOM	430	HZ1	LYS	44	-20.497	18.697	35.555	0.00	0.00	FKBP
ATOM	431	HZ2	LYS	44	-19.853	19.580	36.854	0.00	0.00	FKBP
ATOM	432	HZ3	LYS	44	-21.496	19.168	36.846	0.00	0.00	FKBP
ATOM	433	C	LYS	44	-16.361	15.014	40.049	1.00	17.91	FKBP
ATOM	434	O	LYS	44	-15.928	16.029	40.596	1.00	21.43	FKBP
ATOM	435	N	PRO	45	-15.545	14.014	39.695	1.00	16.30	FKBP
ATOM	436	CD	PRO	45	-15.909	12.612	39.438	1.00	17.34	FKBP
ATOM	437	CA	PRO	45	-14.093	14.182	39.830	1.00	17.48	FKBP
ATOM	438	CB	PRO	45	-13.539	12.779	39.557	1.00	14.90	FKBP
ATOM	439	CG	PRO	45	-14.679	11.871	39.886	1.00	19.40	FKBP
ATOM	440	C	PRO	45	-13.496	15.228	38.887	1.00	15.55	FKBP
ATOM	441	O	PRO	45	-13.942	15.399	37.753	1.00	17.90	FKBP
ATOM	442	N	PHE	46	-12.501	15.942	39.389	1.00	11.92	FKBP
ATOM	443	H	PHE	46	-12.151	15.695	40.268	0.00	0.00	FKBP
ATOM	444	CA	PHE	46	-11.825	16.989	38.637	1.00	10.26	FKBP
ATOM	445	CB	PHE	46	-11.346	18.068	39.615	1.00	7.26	FKBP
ATOM	446	CG	PHE	46	-10.549	19.165	38.980	1.00	2.00	FKBP
ATOM	447	CD1	PHE	46	-9.192	19.284	39.246	1.00	2.00	FKBP
ATOM	448	CD2	PHE	46	-11.180	20.149	38.222	1.00	2.00	FKBP
ATOM	449	CE1	PHE	46	-8.472	20.369	38.779	1.00	2.30	FKBP
ATOM	450	CE2	PHE	46	-10.475	21.243	37.749	1.00	2.00	FKBP
ATOM	451	CZ	PHE	46	-9.117	21.357	38.030	1.00	5.96	FKBP
ATOM	452	C	PHE	46	-10.644	16.371	37.898	1.00	10.45	FKBP
ATOM	453	O	PHE	46	-9.984	15.479	38.421	1.00	16.71	FKBP
ATOM	454	N	LYS	47	-10.421	16.782	36.655	1.00	9.72	FKBP
ATOM	455	H	LYS	47	-11.004	17.458	36.253	0.00	0.00	FKBP
ATOM	456	CA	LYS	47	-9.293	16.255	35.893	1.00	4.83	FKBP
ATOM	457	CB	LYS	47	-9.770	15.421	34.700	1.00	5.22	FKBP
ATOM	458	CG	LYS	47	-10.510	14.147	35.058	1.00	8.65	FKBP
ATOM	459	CD	LYS	47	-11.587	13.853	34.032	1.00	11.93	FKBP
ATOM	460	CE	LYS	47	-11.326	12.543	33.312	1.00	10.86	FKBP
ATOM	461	NZ	LYS	47	-11.608	11.397	34.216	1.00	15.06	FKBP
ATOM	462	HZ1	LYS	47	-12.594	11.462	34.542	0.00	0.00	FKBP
ATOM	463	HZ2	LYS	47	-10.981	11.442	35.042	0.00	0.00	FKBP
ATOM	464	HZ3	LYS	47	-11.471	10.498	33.712	0.00	0.00	FKBP
ATOM	465	C	LYS	47	-8.435	17.389	35.395	1.00	2.00	FKBP
ATOM	466	O	LYS	47	-8.943	18.449	35.061	1.00	2.00	FKBP

	ATOM	467	N	PHE	48	-7.125	17.205	35.472	1.00	2.00	FKBP
	ATOM	468	H	PHE	48	-6.799	16.438	35.994	0.00	0.00	FKBP
	ATOM	469	CA	PHE	48	-6.191	18.157	34.896	1.00	6.26	FKBP
	ATOM	470	CB	PHE	48	-5.964	19.323	35.875	1.00	2.45	FKBP
	ATOM	471	CG	PHE	48	-4.948	19.036	36.942	1.00	4.20	FKBP
	ATOM	472	CD1	PHE	48	-5.254	18.188	38.005	1.00	2.00	FKBP
	ATOM	473	CD2	PHE	48	-3.650	19.548	36.837	1.00	2.00	FKBP
	ATOM	474	CE1	PHE	48	-4.282	17.837	38.936	1.00	2.00	FKBP
	ATOM	475	CE2	PHE	48	-2.664	19.200	37.769	1.00	2.59	FKBP
	ATOM	476	CZ	PHE	48	-2.983	18.340	38.817	1.00	2.53	FKBP
	ATOM	477	C	PHE	48	-4.866	17.469	34.538	1.00	10.81	FKBP
	ATOM	478	O	PHE	48	-4.480	16.476	35.159	1.00	16.65	FKBP
	ATOM	479	N	MET	49	-4.181	17.984	33.526	1.00	13.39	FKBP
	ATOM	480	H	MET	49	-4.543	18.774	33.084	0.00	0.00	FKBP
	ATOM	481	CA	MET	49	-2.892	17.437	33.113	1.00	16.66	FKBP
	ATOM	482	CB	MET	49	-2.690	17.663	31.614	1.00	22.76	FKBP
	ATOM	483	CG	MET	49	-1.538	16.885	31.016	1.00	32.61	FKBP
	ATOM	484	SD	MET	49	-0.985	17.585	29.454	1.00	46.48	FKBP
	ATOM	485	CE	MET	49	-0.812	16.105	28.435	1.00	45.16	FKBP
	ATOM	486	C	MET	49	-1.768	18.109	33.898	1.00	16.05	FKBP
	ATOM	487	O	MET	49	-1.749	19.332	34.046	1.00	17.38	FKBP
	ATOM	488	N	LEU	50	-0.852	17.314	34.433	1.00	16.03	FKBP
	ATOM	489	H	LEU	50	-0.925	16.348	34.258	0.00	0.00	FKBP
	ATOM	490	CA	LEU	50	0.166	17.848	35.336	1.00	16.25	FKBP
	ATOM	491	CB	LEU	50	0.587	16.777	36.350	1.00	16.08	FKBP
	ATOM	492	CG	LEU	50	1.737	17.151	37.290	1.00	15.77	FKBP
	ATOM	493	CD1	LEU	50	1.189	17.731	38.587	1.00	17.22	FKBP
	ATOM	494	CD2	LEU	50	2.591	15.923	37.561	1.00	17.09	FKBP
	ATOM	495	C	LEU	50	1.398	18.380	34.606	1.00	18.27	FKBP
	ATOM	496	O	LEU	50	2.130	17.629	33.962	1.00	17.62	FKBP
	ATOM	497	N	GLY	51	1.659	19.671	34.773	1.00	24.68	FKBP
	ATOM	498	H	GLY	51	1.071	20.196	35.347	0.00	0.00	FKBP
	ATOM	499	CA	GLY	51	2.832	20.281	34.163	1.00	28.29	FKBP
	ATOM	500	C	GLY	51	2.511	21.451	33.246	1.00	30.06	FKBP
	ATOM	501	O	GLY	51	3.312	22.367	33.092	1.00	31.10	FKBP
	ATOM	502	N	LYS	52	1.283	21.482	32.739	1.00	31.85	FKBP
	ATOM	503	H	LYS	52	0.651	20.805	33.051	0.00	0.00	FKBP
	ATOM	504	CA	LYS	52	0.883	22.452	31.724	1.00	30.54	FKBP
	ATOM	505	CB	LYS	52	-0.281	21.887	30.899	1.00	33.91	FKBP

ATOM	506	CG	LYS	52	-0.110	20.427	30.479	1.00	38.74	FKBP
ATOM	507	CD	LYS	52	1.015	20.263	29.458	1.00	44.12	FKBP
ATOM	508	CE	LYS	52	1.708	18.913	29.584	1.00	44.68	FKBP
ATOM	509	NZ	LYS	52	2.954	18.849	28.767	1.00	46.84	FKBP
ATOM	510	HZ1	LYS	52	3.632	19.546	29.134	0.00	0.00	FKBP
ATOM	511	HZ2	LYS	52	2.732	19.066	27.773	0.00	0.00	FKBP
ATOM	512	HZ3	LYS	52	3.361	17.895	28.831	0.00	0.00	FKBP
ATOM	513	C	LYS	52	0.475	23.795	32.323	1.00	27.06	FKBP
ATOM	514	O	LYS	52	-0.349	24.498	31.741	1.00	30.79	FKBP
ATOM	515	N	GLN	53	1.025	24.130	33.490	1.00	21.58	FKBP
ATOM	516	H	GLN	53	1.847	23.671	33.747	0.00	0.00	FKBP
ATOM	517	CA	GLN	53	0.572	25.282	34.279	1.00	18.83	FKBP
ATOM	518	CB	GLN	53	1.219	26.571	33.768	1.00	25.35	FKBP
ATOM	519	CG	GLN	53	2.599	26.848	34.333	1.00	34.50	FKBP
ATOM	520	CD	GLN	53	3.585	25.737	34.025	1.00	42.12	FKBP
ATOM	521	OE1	GLN	53	3.854	25.432	32.865	1.00	46.61	FKBP
ATOM	522	NE2	GLN	53	4.096	25.098	35.067	1.00	46.53	FKBP
ATOM	523	HE21	GLN	53	3.837	25.352	35.970	0.00	0.00	FKBP
ATOM	524	HE22	GLN	53	4.723	24.391	34.821	0.00	0.00	FKBP
ATOM	525	C	GLN	53	-0.950	25.457	34.313	1.00	15.57	FKBP
ATOM	526	O	GLN	53	-1.456	26.570	34.380	1.00	17.17	FKBP
ATOM	527	N	GLU	54	-1.672	24.344	34.338	1.00	12.00	FKBP
ATOM	528	H	GLU	54	-1.188	23.505	34.304	0.00	0.00	FKBP
ATOM	529	CA	GLU	54	-3.126	24.378	34.306	1.00	6.49	FKBP
ATOM	530	CB	GLU	54	-3.666	23.022	33.878	1.00	6.66	FKBP
ATOM	531	CG	GLU	54	-4.296	23.020	32.516	1.00	4.63	FKBP
ATOM	532	CD	GLU	54	-4.414	21.628	31.960	1.00	11.57	FKBP
ATOM	533	OE1	GLU	54	-3.543	21.242	31.157	1.00	18.19	FKBP
ATOM	534	OE2	GLU	54	-5.339	20.896	32.368	1.00	10.83	FKBP
ATOM	535	C	GLU	54	-3.741	24.762	35.642	1.00	5.69	FKBP
ATOM	536	O	GLU	54	-4.873	25.238	35.696	1.00	4.44	FKBP
ATOM	537	N	VAL	55	-3.035	24.444	36.722	1.00	4.70	FKBP
ATOM	538	H	VAL	55	-2.142	24.084	36.580	0.00	0.00	FKBP
ATOM	539	CA	VAL	55	-3.513	24.731	38.071	1.00	6.95	FKBP
ATOM	540	CB	VAL	55	-3.774	23.446	38.849	1.00	3.43	FKBP
ATOM	541	CG1	VAL	55	-4.995	22.759	38.309	1.00	9.22	FKBP
ATOM	542	CG2	VAL	55	-2.573	22.538	38.761	1.00	2.21	FKBP
ATOM	543	C	VAL	55	-2.500	25.559	38.849	1.00	9.75	FKBP
ATOM	544	O	VAL	55	-1.369	25.737	38.408	1.00	9.34	FKBP

ATOM	545	N	ILE	56	-2.887	26.026	40.031	1.00	12.04	FKBP
ATOM	546	H	ILE	56	-3.799	25.844	40.322	0.00	0.00	FKBP
ATOM	547	CA	ILE	56	-1.964	26.785	40.869	1.00	10.94	FKBP
ATOM	548	CB	ILE	56	-2.674	27.365	42.123	1.00	9.38	FKBP
ATOM	549	CG2	ILE	56	-3.665	28.449	41.701	1.00	9.44	FKBP
ATOM	550	CG1	ILE	56	-3.377	26.263	42.920	1.00	4.02	FKBP
ATOM	551	CD1	ILE	56	-4.003	26.756	44.206	1.00	2.00	FKBP
ATOM	552	C	ILE	56	-0.734	25.962	41.286	1.00	12.55	FKBP
ATOM	553	O	ILE	56	-0.759	24.729	41.270	1.00	15.13	FKBP
ATOM	554	N	ARG	57	0.353	26.651	41.615	1.00	10.58	FKBP
ATOM	555	H	ARG	57	0.284	27.627	41.637	0.00	0.00	FKBP
ATOM	556	CA	ARG	57	1.648	26.013	41.850	1.00	12.39	FKBP
ATOM	557	CB	ARG	57	2.707	27.091	42.058	1.00	13.28	FKBP
ATOM	558	CG	ARG	57	4.115	26.573	42.013	1.00	16.07	FKBP
ATOM	559	CD	ARG	57	5.090	27.708	42.068	1.00	18.63	FKBP
ATOM	560	NE	ARG	57	6.447	27.196	42.189	1.00	29.56	FKBP
ATOM	561	HE	ARG	57	6.567	26.228	42.278	0.00	0.00	FKBP
ATOM	562	CZ	ARG	57	7.535	27.957	42.208	1.00	29.74	FKBP
ATOM	563	NH1	ARG	57	8.728	27.390	42.332	1.00	34.84	FKBP
ATOM	564	HH11	ARG	57	8.794	26.398	42.443	0.00	0.00	FKBP
ATOM	565	HH12	ARG	57	9.551	27.954	42.380	0.00	0.00	FKBP
ATOM	566	NH2	ARG	57	7.430	29.277	42.124	1.00	24.22	FKBP
ATOM	567	HH21	ARG	57	6.534	29.712	42.038	0.00	0.00	FKBP
ATOM	568	HH22	ARG	57	8.258	29.836	42.149	0.00	0.00	FKBP
ATOM	569	C	ARG	57	1.700	25.006	43.014	1.00	15.27	FKBP
ATOM	570	O	ARG	57	2.321	23.946	42.901	1.00	16.77	FKBP
ATOM	571	N	GLY	58	1.084	25.349	44.142	1.00	13.48	FKBP
ATOM	572	H	GLY	58	0.719	26.253	44.227	0.00	0.00	FKBP
ATOM	573	CA	GLY	58	0.973	24.402	45.240	1.00	12.25	FKBP
ATOM	574	C	GLY	58	0.326	23.080	44.849	1.00	9.23	FKBP
ATOM	575	O	GLY	58	0.633	22.043	45.438	1.00	8.04	FKBP
ATOM	576	N	TRP	59	-0.567	23.124	43.856	1.00	6.52	FKBP
ATOM	577	H	TRP	59	-0.838	24.004	43.525	0.00	0.00	FKBP
ATOM	578	CA	TRP	59	-1.177	21.927	43.269	1.00	2.00	FKBP
ATOM	579	CB	TRP	59	-2.399	22.294	42.443	1.00	2.00	FKBP
ATOM	580	CG	TRP	59	-3.672	22.138	43.172	1.00	2.87	FKBP
ATOM	581	CD2	TRP	59	-4.707	21.189	42.889	1.00	4.49	FKBP
ATOM	582	CE2	TRP	59	-5.725	21.386	43.843	1.00	5.98	FKBP
ATOM	583	CE3	TRP	59	-4.874	20.193	41.921	1.00	2.00	FKBP

ATOM	584	CD1	TRP	59	-4.093	22.857	44.252	1.00	2.00	FKBP
ATOM	585	NE1	TRP	59	-5.327	22.413	44.659	1.00	4.48	FKBP
ATOM	586	HE1	TRP	59	-5.830	22.768	45.422	0.00	0.00	FKBP
ATOM	587	CZ2	TRP	59	-6.897	20.615	43.859	1.00	7.28	FKBP
ATOM	588	CZ3	TRP	59	-6.043	19.433	41.939	1.00	4.10	FKBP
ATOM	589	CH2	TRP	59	-7.033	19.648	42.900	1.00	2.01	FKBP
ATOM	590	C	TRP	59	-0.215	21.196	42.365	1.00	3.20	FKBP
ATOM	591	O	TRP	59	-0.186	19.969	42.345	1.00	9.79	FKBP
ATOM	592	N	GLU	60	0.507	21.955	41.550	1.00	3.19	FKBP
ATOM	593	H	GLU	60	0.323	22.919	41.539	0.00	0.00	FKBP
ATOM	594	CA	GLU	60	1.484	21.388	40.636	1.00	5.73	FKBP
ATOM	595	CB	GLU	60	2.142	22.502	39.819	1.00	10.18	FKBP
ATOM	596	CG	GLU	60	2.585	22.086	38.415	1.00	13.55	FKBP
ATOM	597	CD	GLU	60	1.463	22.147	37.398	1.00	16.71	FKBP
ATOM	598	OE1	GLU	60	1.649	22.793	36.348	1.00	22.45	FKBP
ATOM	599	OE2	GLU	60	0.393	21.551	37.640	1.00	19.83	FKBP
ATOM	600	C	GLU	60	2.538	20.587	41.395	1.00	8.89	FKBP
ATOM	601	O	GLU	60	2.703	19.395	41.150	1.00	14.67	FKBP
ATOM	602	N	GLU	61	3.116	21.189	42.428	1.00	11.93	FKBP
ATOM	603	H	GLU	61	2.859	22.117	42.606	0.00	0.00	FKBP
ATOM	604	CA	GLU	61	4.123	20.510	43.249	1.00	15.22	FKBP
ATOM	605	CB	GLU	61	5.053	21.533	43.916	1.00	18.18	FKBP
ATOM	606	CG	GLU	61	5.177	22.868	43.171	1.00	28.20	FKBP
ATOM	607	CD	GLU	61	6.615	23.314	42.926	1.00	31.43	FKBP
ATOM	608	OE1	GLU	61	7.478	23.101	43.807	1.00	35.07	FKBP
ATOM	609	OE2	GLU	61	6.865	23.933	41.867	1.00	34.62	FKBP
ATOM	610	C	GLU	61	3.519	19.581	44.315	1.00	14.96	FKBP
ATOM	611	O	GLU	61	4.101	18.558	44.663	1.00	21.59	FKBP
ATOM	612	N	GLY	62	2.355	19.938	44.840	1.00	16.29	FKBP
ATOM	613	H	GLY	62	1.970	20.809	44.617	0.00	0.00	FKBP
ATOM	614	CA	GLY	62	1.687	19.077	45.801	1.00	12.82	FKBP
ATOM	615	C	GLY	62	1.281	17.734	45.219	1.00	12.55	FKBP
ATOM	616	O	GLY	62	1.782	16.697	45.639	1.00	12.58	FKBP
ATOM	617	N	VAL	63	0.438	17.764	44.190	1.00	12.60	FKBP
ATOM	618	H	VAL	63	0.172	18.639	43.830	0.00	0.00	FKBP
ATOM	619	CA	VAL	63	-0.092	16.550	43.570	1.00	12.62	FKBP
ATOM	620	CB	VAL	63	-1.164	16.899	42.511	1.00	7.73	FKBP
ATOM	621	CG1	VAL	63	-1.788	15.628	41.954	1.00	7.25	FKBP
ATOM	622	CG2	VAL	63	-2.234	17.780	43.122	1.00	3.26	FKBP

	ATOM	623	C	VAL	63	0.996	15.674	42.921	1.00	15.97	FKBP
	ATOM	624	O	VAL	63	0.927	14.446	42.958	1.00	18.69	FKBP
	ATOM	625	N	ALA	64	2.048	16.305	42.416	1.00	15.67	FKBP
	ATOM	626	H	ALA	64	2.009	17.279	42.315	0.00	0.00	FKBP
5	ATOM	627	CA	ALA	64	3.196	15.570	41.905	1.00	14.59	FKBP
	ATOM	628	CB	ALA	64	4.201	16.542	41.338	1.00	13.86	FKBP
	ATOM	629	C	ALA	64	3.856	14.687	42.976	1.00	16.87	FKBP
	ATOM	630	O	ALA	64	4.548	13.726	42.656	1.00	19.52	FKBP
	ATOM	631	N	GLN	65	3.657	15.026	44.245	1.00	16.81	FKBP
10	ATOM	632	H	GLN	65	3.161	15.844	44.449	0.00	0.00	FKBP
	ATOM	633	CA	GLN	65	4.202	14.233	45.353	1.00	14.57	FKBP
	ATOM	634	CB	GLN	65	4.359	15.097	46.606	1.00	15.78	FKBP
	ATOM	635	CG	GLN	65	5.473	16.118	46.542	1.00	27.03	FKBP
	ATOM	636	CD	GLN	65	5.524	16.996	47.782	1.00	35.69	FKBP
15	ATOM	637	OE1	GLN	65	5.543	16.500	48.910	1.00	39.86	FKBP
	ATOM	638	NE2	GLN	65	5.516	18.307	47.580	1.00	36.82	FKBP
	ATOM	639	HE21	GLN	65	5.428	18.638	46.667	0.00	0.00	FKBP
	ATOM	640	HE22	GLN	65	5.596	18.845	48.387	0.00	0.00	FKBP
	ATOM	641	C	GLN	65	3.325	13.037	45.706	1.00	11.92	FKBP
20	ATOM	642	O	GLN	65	3.694	12.226	46.553	1.00	12.99	FKBP
	ATOM	643	N	MET	66	2.094	13.034	45.210	1.00	8.83	FKBP
	ATOM	644	H	MET	66	1.872	13.655	44.491	0.00	0.00	FKBP
	ATOM	645	CA	MET	66	1.119	12.044	45.646	1.00	9.40	FKBP
	ATOM	646	CB	MET	66	-0.286	12.651	45.616	1.00	5.56	FKBP
25	ATOM	647	CG	MET	66	-0.487	13.766	46.628	1.00	3.07	FKBP
	ATOM	648	SD	MET	66	-2.084	14.610	46.495	1.00	12.38	FKBP
	ATOM	649	CE	MET	66	-3.186	13.301	46.911	1.00	12.15	FKBP
	ATOM	650	C	MET	66	1.186	10.788	44.774	1.00	13.38	FKBP
	ATOM	651	O	MET	66	1.705	10.831	43.660	1.00	16.22	FKBP
30	ATOM	652	N	SER	67	0.832	9.643	45.346	1.00	13.44	FKBP
	ATOM	653	H	SER	67	0.710	9.638	46.319	0.00	0.00	FKBP
	ATOM	654	CA	SER	67	0.727	8.409	44.565	1.00	11.42	FKBP
	ATOM	655	CB	SER	67	1.649	7.317	45.134	1.00	7.60	FKBP
	ATOM	656	OG	SER	67	1.250	6.897	46.427	1.00	7.91	FKBP
35	ATOM	657	HG	SER	67	1.986	7.045	47.038	0.00	0.00	FKBP
	ATOM	658	C	SER	67	-0.721	7.926	44.518	1.00	12.45	FKBP
	ATOM	659	O	SER	67	-1.556	8.364	45.309	1.00	14.85	FKBP
	ATOM	660	N	VAL	68	-1.055	7.115	43.523	1.00	12.38	FKBP
	ATOM	661	H	VAL	68	-0.361	6.855	42.883	0.00	0.00	FKBP

ATOM	662	CA	VAL	68	-2.457	6.756	43.314	1.00	10.06	FKBP
ATOM	663	CB	VAL	68	-2.647	5.854	42.067	1.00	5.10	FKBP
ATOM	664	CG1	VAL	68	-4.130	5.630	41.800	1.00	5.86	FKBP
ATOM	665	CG2	VAL	68	-2.010	6.489	40.874	1.00	2.65	FKBP
ATOM	666	C	VAL	68	-3.080	6.069	44.532	1.00	9.51	FKBP
ATOM	667	O	VAL	68	-2.603	5.033	44.999	1.00	13.72	FKBP
ATOM	668	N	GLY	69	-4.190	6.630	44.992	1.00	7.92	FKBP
ATOM	669	H	GLY	69	-4.587	7.362	44.469	0.00	0.00	FKBP
ATOM	670	CA	GLY	69	-4.872	6.114	46.162	1.00	8.54	FKBP
ATOM	671	C	GLY	69	-4.755	7.061	47.344	1.00	7.63	FKBP
ATOM	672	O	GLY	69	-5.649	7.132	48.185	1.00	12.92	FKBP
ATOM	673	N	GLN	70	-3.694	7.859	47.354	1.00	3.17	FKBP
ATOM	674	H	GLN	70	-3.135	7.917	46.548	0.00	0.00	FKBP
ATOM	675	CA	GLN	70	-3.357	8.660	48.515	1.00	2.00	FKBP
ATOM	676	CB	GLN	70	-1.927	9.161	48.395	1.00	2.57	FKBP
ATOM	677	CG	GLN	70	-1.483	10.064	49.524	1.00	10.26	FKBP
ATOM	678	CD	GLN	70	-0.066	10.555	49.331	1.00	10.61	FKBP
ATOM	679	OE1	GLN	70	0.673	10.028	48.505	1.00	18.69	FKBP
ATOM	680	NE2	GLN	70	0.310	11.586	50.067	1.00	11.45	FKBP
ATOM	681	HE21	GLN	70	-0.298	11.997	50.702	0.00	0.00	FKBP
ATOM	682	HE22	GLN	70	1.237	11.850	49.896	0.00	0.00	FKBP
ATOM	683	C	GLN	70	-4.299	9.830	48.671	1.00	2.00	FKBP
ATOM	684	O	GLN	70	-4.749	10.400	47.691	1.00	3.88	FKBP
ATOM	685	N	ARG	71	-4.711	10.082	49.904	1.00	5.36	FKBP
ATOM	686	H	ARG	71	-4.639	9.362	50.543	0.00	0.00	FKBP
ATOM	687	CA	ARG	71	-5.486	11.274	50.246	1.00	5.53	FKBP
ATOM	688	CB	ARG	71	-6.753	10.873	50.997	1.00	2.00	FKBP
ATOM	689	CG	ARG	71	-7.697	12.010	51.228	1.00	2.00	FKBP
ATOM	690	CD	ARG	71	-9.066	11.504	51.639	1.00	3.25	FKBP
ATOM	691	NE	ARG	71	-9.812	12.542	52.347	1.00	8.85	FKBP
ATOM	692	HE	ARG	71	-9.309	13.289	52.735	0.00	0.00	FKBP
ATOM	693	CZ	ARG	71	-11.134	12.564	52.475	1.00	18.29	FKBP
ATOM	694	NH1	ARG	71	-11.708	13.525	53.183	1.00	25.79	FKBP
ATOM	695	HH11	ARG	71	-11.149	14.237	53.609	0.00	0.00	FKBP
ATOM	696	HH12	ARG	71	-12.702	13.542	53.282	0.00	0.00	FKBP
ATOM	697	NH2	ARG	71	-11.888	11.640	51.890	1.00	23.05	FKBP
ATOM	698	HH21	ARG	71	-11.460	10.906	51.361	0.00	0.00	FKBP
ATOM	699	HH22	ARG	71	-12.879	11.654	52.011	0.00	0.00	FKBP
ATOM	700	C	ARG	71	-4.650	12.208	51.114	1.00	3.03	FKBP

	ATOM	701	O	ARG	71	-4.006	11.764	52.060	1.00	4.39	FKBP
	ATOM	702	N	ALA	72	-4.628	13.489	50.774	1.00	2.46	FKBP
	ATOM	703	H	ALA	72	-5.218	13.805	50.054	0.00	0.00	FKBP
	ATOM	704	CA	ALA	72	-3.725	14.428	51.425	1.00	2.00	FKBP
5	ATOM	705	CB	ALA	72	-2.456	14.557	50.636	1.00	2.00	FKBP
	ATOM	706	C	ALA	72	-4.326	15.803	51.654	1.00	4.21	FKBP
	ATOM	707	O	ALA	72	-5.376	16.145	51.119	1.00	10.57	FKBP
	ATOM	708	N	LYS	73	-3.766	16.490	52.632	1.00	8.68	FKBP
	ATOM	709	H	LYS	73	-3.101	16.042	53.199	0.00	0.00	FKBP
10	ATOM	710	CA	LYS	73	-4.121	17.861	52.917	1.00	4.13	FKBP
	ATOM	711	CB	LYS	73	-4.387	18.018	54.410	1.00	6.40	FKBP
	ATOM	712	CG	LYS	73	-4.104	19.408	54.956	1.00	13.82	FKBP
	ATOM	713	CD	LYS	73	-4.807	19.628	56.287	1.00	15.85	FKBP
	ATOM	714	CE	LYS	73	-4.136	20.729	57.086	1.00	18.32	FKBP
15	ATOM	715	NZ	LYS	73	-5.033	21.240	58.148	1.00	22.33	FKBP
	ATOM	716	HZ1	LYS	73	-5.238	20.469	58.817	0.00	0.00	FKBP
	ATOM	717	HZ2	LYS	73	-5.920	21.583	57.728	0.00	0.00	FKBP
	ATOM	718	HZ3	LYS	73	-4.569	22.019	58.657	0.00	0.00	FKBP
	ATOM	719	C	LYS	73	-2.943	18.713	52.488	1.00	4.72	FKBP
20	ATOM	720	O	LYS	73	-1.794	18.396	52.814	1.00	6.20	FKBP
	ATOM	721	N	LEU	74	-3.212	19.628	51.566	1.00	6.47	FKBP
	ATOM	722	H	LEU	74	-4.064	19.565	51.121	0.00	0.00	FKBP
	ATOM	723	CA	LEU	74	-2.218	20.582	51.082	1.00	8.06	FKBP
	ATOM	724	CB	LEU	74	-2.303	20.706	49.560	1.00	12.85	FKBP
25	ATOM	725	CG	LEU	74	-1.440	19.791	48.695	1.00	11.86	FKBP
	ATOM	726	CD1	LEU	74	-1.789	18.330	48.947	1.00	11.50	FKBP
	ATOM	727	CD2	LEU	74	-1.663	20.157	47.241	1.00	12.57	FKBP
	ATOM	728	C	LEU	74	-2.403	21.962	51.695	1.00	8.90	FKBP
	ATOM	729	O	LEU	74	-3.449	22.600	51.515	1.00	14.56	FKBP
30	ATOM	730	N	THR	75	-1.385	22.431	52.405	1.00	7.32	FKBP
	ATOM	731	H	THR	75	-0.717	21.784	52.717	0.00	0.00	FKBP
	ATOM	732	CA	THR	75	-1.383	23.796	52.913	1.00	6.76	FKBP
	ATOM	733	CB	THR	75	-0.905	23.830	54.397	1.00	6.87	FKBP
	ATOM	734	OG1	THR	75	-1.957	23.327	55.227	1.00	2.01	FKBP
35	ATOM	735	HG1	THR	75	-2.720	23.901	55.117	0.00	0.00	FKBP
	ATOM	736	CG2	THR	75	-0.556	25.238	54.861	1.00	3.73	FKBP
	ATOM	737	C	THR	75	-0.513	24.654	52.000	1.00	6.27	FKBP
	ATOM	738	O	THR	75	0.683	24.416	51.846	1.00	5.48	FKBP
	ATOM	739	N	ILE	76	-1.180	25.508	51.234	1.00	10.43	FKBP

	ATOM	740	H	ILE	76	-2.141	25.633	51.388	0.00	0.00	FKBP
	ATOM	741	CA	ILE	76	-0.542	26.284	50.167	1.00	11.16	FKBP
	ATOM	742	CB	ILE	76	-1.326	26.090	48.830	1.00	6.31	FKBP
	ATOM	743	CG2	ILE	76	-0.653	26.827	47.719	1.00	9.44	FKBP
	ATOM	744	CG1	ILE	76	-1.388	24.601	48.459	1.00	5.62	FKBP
	ATOM	745	CD1	ILE	76	-2.630	24.205	47.691	1.00	2.00	FKBP
	ATOM	746	C	ILE	76	-0.454	27.788	50.522	1.00	12.21	FKBP
	ATOM	747	O	ILE	76	-1.476	28.460	50.752	1.00	13.89	FKBP
	ATOM	748	N	SER	77	0.768	28.287	50.692	1.00	10.50	FKBP
	ATOM	749	H	SER	77	1.535	27.692	50.566	0.00	0.00	FKBP
	ATOM	750	CA	SER	77	0.947	29.700	51.009	1.00	11.73	FKBP
	ATOM	751	CB	SER	77	2.354	29.978	51.571	1.00	11.33	FKBP
	ATOM	752	OG	SER	77	3.405	29.669	50.667	1.00	18.57	FKBP
	ATOM	753	HG	SER	77	4.140	30.103	51.109	0.00	0.00	FKBP
	ATOM	754	C	SER	77	0.681	30.566	49.790	1.00	12.45	FKBP
	ATOM	755	O	SER	77	0.922	30.149	48.662	1.00	15.48	FKBP
	ATOM	756	N	PRO	78	0.151	31.778	49.998	1.00	14.32	FKBP
	ATOM	757	CD	PRO	78	0.192	32.544	51.251	1.00	18.10	FKBP
	ATOM	758	CA	PRO	78	-0.362	32.607	48.906	1.00	14.95	FKBP
	ATOM	759	CB	PRO	78	-0.594	33.957	49.573	1.00	15.74	FKBP
	ATOM	760	CG	PRO	78	0.309	33.944	50.759	1.00	15.85	FKBP
	ATOM	761	C	PRO	78	0.574	32.728	47.710	1.00	15.21	FKBP
	ATOM	762	O	PRO	78	0.109	32.790	46.576	1.00	20.63	FKBP
	ATOM	763	N	ASP	79	1.882	32.698	47.956	1.00	13.60	FKBP
	ATOM	764	H	ASP	79	2.162	32.697	48.889	0.00	0.00	FKBP
	ATOM	765	CA	ASP	79	2.877	32.679	46.874	1.00	19.42	FKBP
	ATOM	766	CB	ASP	79	4.305	32.510	47.424	1.00	28.97	FKBP
	ATOM	767	CG	ASP	79	4.599	33.401	48.629	1.00	37.43	FKBP
	ATOM	768	OD1	ASP	79	5.657	33.195	49.270	1.00	39.71	FKBP
	ATOM	769	OD2	ASP	79	3.792	34.306	48.939	1.00	45.91	FKBP
	ATOM	770	C	ASP	79	2.616	31.548	45.877	1.00	17.87	FKBP
	ATOM	771	O	ASP	79	2.547	31.777	44.676	1.00	20.31	FKBP
	ATOM	772	N	TYR	80	2.442	30.335	46.392	1.00	15.45	FKBP
	ATOM	773	H	TYR	80	2.347	30.254	47.356	0.00	0.00	FKBP
	ATOM	774	CA	TYR	80	2.142	29.178	45.557	1.00	12.31	FKBP
	ATOM	775	CB	TYR	80	2.611	27.897	46.234	1.00	10.17	FKBP
	ATOM	776	CG	TYR	80	4.082	27.626	46.070	1.00	9.13	FKBP
	ATOM	777	CD1	TYR	80	5.022	28.600	46.373	1.00	5.08	FKBP
	ATOM	778	CE1	TYR	80	6.373	28.303	46.419	1.00	6.16	FKBP

	ATOM	779	CD2	TYR	80	4.536	26.347	45.781	1.00	12.62	FKBP
	ATOM	780	CE2	TYR	80	5.889	26.037	45.827	1.00	15.72	FKBP
	ATOM	781	CZ	TYR	80	6.801	27.021	46.159	1.00	13.97	FKBP
	ATOM	782	OH	TYR	80	8.124	26.683	46.343	1.00	19.55	FKBP
5	ATOM	783	HH	TYR	80	8.729	27.408	46.126	0.00	0.00	FKBP
	ATOM	784	C	TYR	80	0.657	29.033	45.227	1.00	9.68	FKBP
	ATOM	785	O	TYR	80	0.194	27.936	44.907	1.00	9.28	FKBP
	ATOM	786	N	ALA	81	-0.104	30.115	45.344	1.00	9.06	FKBP
	ATOM	787	H	ALA	81	0.347	31.010	45.423	0.00	0.00	FKBP
10	ATOM	788	CA	ALA	81	-1.536	30.071	45.028	1.00	8.94	FKBP
	ATOM	789	CB	ALA	81	-2.362	29.899	46.312	1.00	10.95	FKBP
	ATOM	790	C	ALA	81	-1.973	31.342	44.290	1.00	11.59	FKBP
	ATOM	791	O	ALA	81	-1.507	31.630	43.192	1.00	14.63	FKBP
	ATOM	792	N	TYR	82	-2.886	32.106	44.874	1.00	13.59	FKBP
15	ATOM	793	H	TYR	82	-3.142	32.049	45.838	0.00	0.00	FKBP
	ATOM	794	CA	TYR	82	-3.462	33.239	44.147	1.00	15.87	FKBP
	ATOM	795	CB	TYR	82	-4.982	33.249	44.324	1.00	15.49	FKBP
	ATOM	796	CG	TYR	82	-5.676	32.084	43.658	1.00	19.64	FKBP
	ATOM	797	CD1	TYR	82	-6.283	31.091	44.415	1.00	18.02	FKBP
20	ATOM	798	CE1	TYR	82	-6.918	30.013	43.804	1.00	16.50	FKBP
	ATOM	799	CD2	TYR	82	-5.724	31.975	42.262	1.00	19.36	FKBP
	ATOM	800	CE2	TYR	82	-6.357	30.904	41.648	1.00	12.44	FKBP
	ATOM	801	CZ	TYR	82	-6.946	29.930	42.425	1.00	12.60	FKBP
	ATOM	802	OH	TYR	82	-7.546	28.871	41.800	1.00	12.06	FKBP
25	ATOM	803	HH	TYR	82	-7.818	28.255	42.478	0.00	0.00	FKBP
	ATOM	804	C	TYR	82	-2.869	34.591	44.552	1.00	15.70	FKBP
	ATOM	805	O	TYR	82	-3.388	35.646	44.183	1.00	15.54	FKBP
	ATOM	806	N	GLY	83	-1.763	34.539	45.288	1.00	17.13	FKBP
	ATOM	807	H	GLY	83	-1.475	33.662	45.571	0.00	0.00	FKBP
30	ATOM	808	CA	GLY	83	-0.972	35.719	45.566	1.00	15.64	FKBP
	ATOM	809	C	GLY	83	-1.681	36.878	46.233	1.00	20.32	FKBP
	ATOM	810	O	GLY	83	-2.708	36.728	46.910	1.00	23.74	FKBP
	ATOM	811	N	ALA	84	-1.099	38.055	46.055	1.00	19.06	FKBP
	ATOM	812	H	ALA	84	-0.306	38.078	45.480	0.00	0.00	FKBP
35	ATOM	813	CA	ALA	84	-1.639	39.270	46.628	1.00	15.70	FKBP
	ATOM	814	CB	ALA	84	-0.640	40.394	46.455	1.00	19.93	FKBP
	ATOM	815	C	ALA	84	-2.965	39.637	45.982	1.00	13.85	FKBP
	ATOM	816	O	ALA	84	-3.823	40.230	46.618	1.00	14.46	FKBP
	ATOM	817	N	THR	85	-3.131	39.247	44.726	1.00	17.88	FKBP

ATOM	818	H	THR	85	-2.470	38.659	44.303	0.00	0.00	FKBP
ATOM	819	CA	THR	85	-4.308	39.623	43.934	1.00	24.03	FKBP
ATOM	820	CB	THR	85	-4.036	39.482	42.419	1.00	21.29	FKBP
ATOM	821	OG1	THR	85	-3.482	38.185	42.150	1.00	28.80	FKBP
ATOM	822	HG1	THR	85	-4.132	37.483	42.316	0.00	0.00	FKBP
ATOM	823	CG2	THR	85	-3.054	40.541	41.956	1.00	16.23	FKBP
ATOM	824	C	THR	85	-5.537	38.787	44.254	1.00	24.35	FKBP
ATOM	825	O	THR	85	-6.660	39.189	43.954	1.00	27.70	FKBP
ATOM	826	N	GLY	86	-5.304	37.579	44.761	1.00	25.09	FKBP
ATOM	827	H	GLY	86	-4.382	37.292	44.914	0.00	0.00	FKBP
ATOM	828	CA	GLY	86	-6.388	36.655	45.020	1.00	19.79	FKBP
ATOM	829	C	GLY	86	-7.151	36.310	43.759	1.00	21.57	FKBP
ATOM	830	O	GLY	86	-6.589	36.200	42.659	1.00	18.32	FKBP
ATOM	831	N	HIS	87	-8.454	36.149	43.930	1.00	21.72	FKBP
ATOM	832	H	HIS	87	-8.780	36.318	44.827	0.00	0.00	FKBP
ATOM	833	CA	HIS	87	-9.355	35.858	42.828	1.00	24.25	FKBP
ATOM	834	CB	HIS	87	-9.432	34.350	42.568	1.00	25.61	FKBP
ATOM	835	CG	HIS	87	-10.134	33.994	41.292	1.00	29.60	FKBP
ATOM	836	CD2	HIS	87	-11.360	33.466	41.064	1.00	27.65	FKBP
ATOM	837	ND1	HIS	87	-9.564	34.185	40.050	1.00	31.39	FKBP
ATOM	838	HD1	HIS	87	-8.690	34.592	39.843	0.00	0.00	FKBP
ATOM	839	CE1	HIS	87	-10.405	33.783	39.115	1.00	32.76	FKBP
ATOM	840	NE2	HIS	87	-11.503	33.347	39.703	1.00	30.12	FKBP
ATOM	841	HE2	HIS	87	-12.329	33.167	39.202	0.00	0.00	FKBP
ATOM	842	C	HIS	87	-10.727	36.387	43.212	1.00	22.13	FKBP
ATOM	843	O	HIS	87	-11.356	35.891	44.152	1.00	27.18	FKBP
ATOM	844	N	PRO	88	-11.105	37.531	42.639	1.00	19.63	FKBP
ATOM	845	CD	PRO	88	-10.357	38.290	41.620	1.00	20.36	FKBP
ATOM	846	CA	PRO	88	-11.989	38.403	43.410	1.00	18.79	FKBP
ATOM	847	CB	PRO	88	-11.946	39.707	42.626	1.00	18.51	FKBP
ATOM	848	CG	PRO	88	-10.550	39.713	42.059	1.00	16.30	FKBP
ATOM	849	C	PRO	88	-13.399	37.848	43.580	1.00	18.22	FKBP
ATOM	850	O	PRO	88	-13.974	37.286	42.650	1.00	21.77	FKBP
ATOM	851	N	GLY	89	-13.851	37.819	44.828	1.00	15.16	FKBP
ATOM	852	H	GLY	89	-13.303	38.201	45.539	0.00	0.00	FKBP
ATOM	853	CA	GLY	89	-15.160	37.271	45.120	1.00	12.28	FKBP
ATOM	854	C	GLY	89	-15.116	35.891	45.749	1.00	13.88	FKBP
ATOM	855	O	GLY	89	-16.142	35.385	46.211	1.00	13.05	FKBP
ATOM	856	N	ILE	90	-13.932	35.289	45.812	1.00	12.11	FKBP

ATOM	857	H	ILE	90	-13.164	35.742	45.410	0.00	0.00	FKBP
ATOM	858	CA	ILE	90	-13.831	33.928	46.328	1.00	17.75	FKBP
ATOM	859	CB	ILE	90	-13.950	32.875	45.177	1.00	23.54	FKBP
ATOM	860	CG2	ILE	90	-13.063	33.252	44.007	1.00	24.28	FKBP
ATOM	861	CG1	ILE	90	-13.590	31.478	45.688	1.00	28.28	FKBP
ATOM	862	CD1	ILE	90	-14.036	30.361	44.764	1.00	34.25	FKBP
ATOM	863	C	ILE	90	-12.577	33.670	47.150	1.00	14.47	FKBP
ATOM	864	O	ILE	90	-12.663	33.134	48.247	1.00	15.69	FKBP
ATOM	865	N	ILE	91	-11.416	34.013	46.600	1.00	12.99	FKBP
ATOM	866	H	ILE	91	-11.413	34.380	45.696	0.00	0.00	FKBP
ATOM	867	CA	ILE	91	-10.150	33.915	47.328	1.00	9.92	FKBP
ATOM	868	CB	ILE	91	-9.091	33.085	46.559	1.00	6.38	FKBP
ATOM	869	CG2	ILE	91	-7.873	32.881	47.428	1.00	2.00	FKBP
ATOM	870	CG1	ILE	91	-9.681	31.762	46.041	1.00	4.55	FKBP
ATOM	871	CD1	ILE	91	-10.163	30.821	47.084	1.00	3.68	FKBP
ATOM	872	C	ILE	91	-9.584	35.324	47.520	1.00	15.34	FKBP
ATOM	873	O	ILE	91	-9.285	36.025	46.539	1.00	13.98	FKBP
ATOM	874	N	PRO	92	-9.520	35.797	48.781	1.00	17.29	FKBP
ATOM	875	CD	PRO	92	-9.964	35.110	50.011	1.00	14.17	FKBP
ATOM	876	CA	PRO	92	-9.007	37.143	49.062	1.00	12.40	FKBP
ATOM	877	CB	PRO	92	-9.421	37.381	50.514	1.00	10.67	FKBP
ATOM	878	CG	PRO	92	-9.477	36.019	51.107	1.00	11.96	FKBP
ATOM	879	C	PRO	92	-7.492	37.264	48.855	1.00	14.30	FKBP
ATOM	880	O	PRO	92	-6.815	36.290	48.516	1.00	17.48	FKBP
ATOM	881	N	PRO	93	-6.966	38.493	48.923	1.00	15.65	FKBP
ATOM	882	CD	PRO	93	-7.700	39.762	48.785	1.00	18.15	FKBP
ATOM	883	CA	PRO	93	-5.518	38.704	48.833	1.00	16.50	FKBP
ATOM	884	CB	PRO	93	-5.380	40.217	48.941	1.00	17.10	FKBP
ATOM	885	CG	PRO	93	-6.629	40.717	48.308	1.00	22.16	FKBP
ATOM	886	C	PRO	93	-4.743	37.999	49.933	1.00	16.97	FKBP
ATOM	887	O	PRO	93	-5.160	37.971	51.090	1.00	20.11	FKBP
ATOM	888	N	HIS	94	-3.609	37.424	49.563	1.00	15.46	FKBP
ATOM	889	H	HIS	94	-3.476	37.286	48.598	0.00	0.00	FKBP
ATOM	890	CA	HIS	94	-2.701	36.830	50.538	1.00	14.40	FKBP
ATOM	891	CB	HIS	94	-2.366	37.855	51.608	1.00	12.10	FKBP
ATOM	892	CG	HIS	94	-1.762	39.103	51.061	1.00	15.95	FKBP
ATOM	893	CD2	HIS	94	-2.313	40.308	50.781	1.00	16.10	FKBP
ATOM	894	ND1	HIS	94	-0.455	39.165	50.621	1.00	16.58	FKBP
ATOM	895	HD1	HIS	94	0.241	38.484	50.761	0.00	0.00	FKBP

	ATOM	896	CE1	HIS	94	-0.230	40.351	50.086	1.00	20.16	FKBP
	ATOM	897	NE2	HIS	94	-1.342	41.063	50.171	1.00	21.63	FKBP
	ATOM	898	HE2	HIS	94	-1.470	41.979	49.833	0.00	0.00	FKBP
	ATOM	899	C	HIS	94	-3.176	35.531	51.202	1.00	13.30	FKBP
	ATOM	900	O	HIS	94	-2.380	34.843	51.836	1.00	16.61	FKBP
	ATOM	901	N	ALA	95	-4.403	35.112	50.915	1.00	6.56	FKBP
	ATOM	902	H	ALA	95	-4.911	35.568	50.215	0.00	0.00	FKBP
	ATOM	903	CA	ALA	95	-4.982	33.954	51.576	1.00	7.81	FKBP
	ATOM	904	CB	ALA	95	-6.365	33.676	51.026	1.00	2.72	FKBP
	ATOM	905	C	ALA	95	-4.132	32.683	51.516	1.00	10.01	FKBP
	ATOM	906	O	ALA	95	-3.691	32.260	50.456	1.00	10.42	FKBP
	ATOM	907	N	THR	96	-3.801	32.165	52.691	1.00	12.98	FKBP
	ATOM	908	H	THR	96	-3.847	32.758	53.468	0.00	0.00	FKBP
	ATOM	909	CA	THR	96	-3.319	30.797	52.831	1.00	12.92	FKBP
	ATOM	910	CB	THR	96	-2.740	30.568	54.254	1.00	9.93	FKBP
	ATOM	911	OG1	THR	96	-1.655	31.480	54.472	1.00	11.98	FKBP
	ATOM	912	HG1	THR	96	-1.236	31.644	53.620	0.00	0.00	FKBP
	ATOM	913	CG2	THR	96	-2.240	29.139	54.430	1.00	3.68	FKBP
	ATOM	914	C	THR	96	-4.501	29.852	52.600	1.00	14.35	FKBP
	ATOM	915	O	THR	96	-5.569	30.025	53.212	1.00	14.86	FKBP
	ATOM	916	N	LEU	97	-4.349	28.937	51.642	1.00	8.43	FKBP
	ATOM	917	H	LEU	97	-3.495	28.902	51.157	0.00	0.00	FKBP
	ATOM	918	CA	LEU	97	-5.406	27.976	51.332	1.00	3.80	FKBP
	ATOM	919	CB	LEU	97	-5.672	27.930	49.826	1.00	3.61	FKBP
	ATOM	920	CG	LEU	97	-5.948	29.193	49.011	1.00	6.56	FKBP
	ATOM	921	CD1	LEU	97	-5.831	28.841	47.534	1.00	2.62	FKBP
	ATOM	922	CD2	LEU	97	-7.326	29.758	49.318	1.00	6.52	FKBP
	ATOM	923	C	LEU	97	-5.083	26.557	51.814	1.00	5.71	FKBP
	ATOM	924	O	LEU	97	-3.926	26.123	51.815	1.00	7.74	FKBP
	ATOM	925	N	VAL	98	-6.121	25.814	52.167	1.00	2.33	FKBP
	ATOM	926	H	VAL	98	-7.012	26.221	52.183	0.00	0.00	FKBP
	ATOM	927	CA	VAL	98	-5.968	24.407	52.476	1.00	3.09	FKBP
	ATOM	928	CB	VAL	98	-6.461	24.079	53.900	1.00	4.96	FKBP
	ATOM	929	CG1	VAL	98	-6.144	22.638	54.230	1.00	2.00	FKBP
	ATOM	930	CG2	VAL	98	-5.824	25.011	54.917	1.00	2.00	FKBP
	ATOM	931	C	VAL	98	-6.801	23.602	51.491	1.00	7.78	FKBP
	ATOM	932	O	VAL	98	-8.012	23.836	51.346	1.00	8.13	FKBP
	ATOM	933	N	PHE	99	-6.166	22.622	50.853	1.00	7.58	FKBP
	ATOM	934	H	PHE	99	-5.202	22.540	50.970	0.00	0.00	FKBP

ATOM	935	CA	PHE	99	-6.877	21.677	49.996	1.00	6.62	FKBP
ATOM	936	CB	PHE	99	-6.303	21.728	48.578	1.00	2.00	FKBP
ATOM	937	CG	PHE	99	-6.824	22.873	47.763	1.00	4.66	FKBP
ATOM	938	CD1	PHE	99	-6.115	24.070	47.687	1.00	4.09	FKBP
ATOM	939	CD2	PHE	99	-8.069	22.787	47.138	1.00	2.68	FKBP
ATOM	940	CE1	PHE	99	-6.638	25.166	47.008	1.00	2.00	FKBP
ATOM	941	CE2	PHE	99	-8.598	23.874	46.462	1.00	2.00	FKBP
ATOM	942	CZ	PHE	99	-7.879	25.068	46.399	1.00	2.00	FKBP
ATOM	943	C	PHE	99	-6.849	20.239	50.519	1.00	5.20	FKBP
ATOM	944	O	PHE	99	-5.796	19.718	50.860	1.00	5.24	FKBP
ATOM	945	N	ASP	100	-8.014	19.613	50.627	1.00	3.90	FKBP
ATOM	946	H	ASP	100	-8.834	20.147	50.593	0.00	0.00	FKBP
ATOM	947	CA	ASP	100	-8.070	18.167	50.830	1.00	7.59	FKBP
ATOM	948	CB	ASP	100	-9.205	17.817	51.804	1.00	6.95	FKBP
ATOM	949	CG	ASP	100	-9.424	16.310	51.966	1.00	7.89	FKBP
ATOM	950	OD1	ASP	100	-8.564	15.494	51.568	1.00	14.35	FKBP
ATOM	951	OD2	ASP	100	-10.480	15.937	52.511	1.00	12.55	FKBP
ATOM	952	C	ASP	100	-8.280	17.463	49.482	1.00	9.31	FKBP
ATOM	953	O	ASP	100	-9.379	17.490	48.934	1.00	10.21	FKBP
ATOM	954	N	VAL	101	-7.232	16.832	48.954	1.00	9.09	FKBP
ATOM	955	H	VAL	101	-6.416	16.741	49.499	0.00	0.00	FKBP
ATOM	956	CA	VAL	101	-7.306	16.202	47.633	1.00	11.24	FKBP
ATOM	957	CB	VAL	101	-6.417	16.956	46.557	1.00	7.24	FKBP
ATOM	958	CG1	VAL	101	-6.122	18.380	47.014	1.00	5.62	FKBP
ATOM	959	CG2	VAL	101	-5.118	16.208	46.278	1.00	3.42	FKBP
ATOM	960	C	VAL	101	-6.957	14.711	47.652	1.00	12.17	FKBP
ATOM	961	O	VAL	101	-5.962	14.296	48.251	1.00	12.83	FKBP
ATOM	962	N	GLU	102	-7.796	13.913	47.001	1.00	11.69	FKBP
ATOM	963	H	GLU	102	-8.591	14.307	46.611	0.00	0.00	FKBP
ATOM	964	CA	GLU	102	-7.527	12.490	46.813	1.00	14.51	FKBP
ATOM	965	CB	GLU	102	-8.697	11.660	47.356	1.00	12.86	FKBP
ATOM	966	CG	GLU	102	-8.562	10.171	47.074	1.00	18.32	FKBP
ATOM	967	CD	GLU	102	-9.681	9.340	47.666	1.00	20.79	FKBP
ATOM	968	OE1	GLU	102	-10.840	9.811	47.715	1.00	26.66	FKBP
ATOM	969	OE2	GLU	102	-9.402	8.187	48.052	1.00	23.60	FKBP
ATOM	970	C	GLU	102	-7.266	12.132	45.336	1.00	13.17	FKBP
ATOM	971	O	GLU	102	-8.100	12.392	44.465	1.00	15.41	FKBP
ATOM	972	N	LEU	103	-6.147	11.465	45.079	1.00	9.34	FKBP
ATOM	973	H	LEU	103	-5.600	11.178	45.846	0.00	0.00	FKBP

	ATOM	974	CA	LEU	103	-5.763	11.096	43.722	1.00	13.72	FKBP
	ATOM	975	CB	LEU	103	-4.226	11.024	43.593	1.00	6.09	FKBP
	ATOM	976	CG	LEU	103	-3.643	10.842	42.180	1.00	4.19	FKBP
	ATOM	977	CD1	LEU	103	-4.309	11.807	41.220	1.00	8.95	FKBP
5	ATOM	978	CD2	LEU	103	-2.149	11.088	42.180	1.00	3.73	FKBP
	ATOM	979	C	LEU	103	-6.404	9.767	43.302	1.00	15.75	FKBP
	ATOM	980	O	LEU	103	-5.838	8.698	43.511	1.00	16.07	FKBP
	ATOM	981	N	LEU	104	-7.579	9.856	42.685	1.00	18.31	FKBP
	ATOM	982	H	LEU	104	-7.915	10.758	42.502	0.00	0.00	FKBP
10	ATOM	983	CA	LEU	104	-8.342	8.680	42.257	1.00	16.33	FKBP
	ATOM	984	CB	LEU	104	-9.664	9.120	41.633	1.00	14.17	FKBP
	ATOM	985	CG	LEU	104	-10.547	10.017	42.500	1.00	14.18	FKBP
	ATOM	986	CD1	LEU	104	-11.838	10.345	41.772	1.00	13.42	FKBP
	ATOM	987	CD2	LEU	104	-10.843	9.307	43.804	1.00	14.17	FKBP
15	ATOM	988	C	LEU	104	-7.594	7.786	41.266	1.00	18.03	FKBP
	ATOM	989	O	LEU	104	-7.390	6.599	41.516	1.00	18.22	FKBP
	ATOM	990	N	LYS	105	-7.196	8.360	40.134	1.00	20.74	FKBP
	ATOM	991	H	LYS	105	-7.343	9.323	40.023	0.00	0.00	FKBP
	ATOM	992	CA	LYS	105	-6.510	7.603	39.086	1.00	20.67	FKBP
20	ATOM	993	CB	LYS	105	-7.529	6.806	38.263	1.00	24.07	FKBP
	ATOM	994	CG	LYS	105	-8.765	7.605	37.853	1.00	27.58	FKBP
	ATOM	995	CD	LYS	105	-9.733	6.771	37.027	1.00	30.34	FKBP
	ATOM	996	CE	LYS	105	-10.994	7.557	36.684	1.00	34.49	FKBP
	ATOM	997	NZ	LYS	105	-11.853	7.826	37.876	1.00	35.90	FKBP
25	ATOM	998	HZ1	LYS	105	-11.317	8.378	38.576	0.00	0.00	FKBP
	ATOM	999	HZ2	LYS	105	-12.151	6.928	38.306	0.00	0.00	FKBP
	ATOM	1000	HZ3	LYS	105	-12.690	8.371	37.584	0.00	0.00	FKBP
	ATOM	1001	C	LYS	105	-5.692	8.497	38.154	1.00	19.89	FKBP
	ATOM	1002	O	LYS	105	-5.948	9.696	38.038	1.00	21.43	FKBP
30	ATOM	1003	N	LEU	106	-4.664	7.927	37.545	1.00	22.51	FKBP
	ATOM	1004	H	LEU	106	-4.392	7.031	37.820	0.00	0.00	FKBP
	ATOM	1005	CA	LEU	106	-4.015	8.575	36.411	1.00	24.63	FKBP
	ATOM	1006	CB	LEU	106	-2.500	8.385	36.469	1.00	20.64	FKBP
	ATOM	1007	CG	LEU	106	-1.709	9.334	37.369	1.00	25.07	FKBP
35	ATOM	1008	CD1	LEU	106	-2.201	10.771	37.213	1.00	26.33	FKBP
	ATOM	1009	CD2	LEU	106	-1.853	8.891	38.791	1.00	25.85	FKBP
	ATOM	1010	C	LEU	106	-4.544	8.044	35.076	1.00	27.28	FKBP
	ATOM	1011	O	LEU	106	-4.969	6.887	34.978	1.00	30.28	FKBP
	ATOM	1012	N	GLU	107	-4.660	8.946	34.108	1.00	28.70	FKBP

	ATOM	1013	H	GLU	107	-4.585	9.896	34.325	0.00	0.00	FKBP
	ATOM	1014	CA	GLU	107	-4.910	8.585	32.718	1.00	28.85	FKBP
	ATOM	1015	CB	GLU	107	-6.410	8.650	32.415	1.00	24.83	FKBP
	ATOM	1016	CG	GLU	107	-7.125	9.812	33.068	1.00	28.14	FKBP
5	ATOM	1017	CD	GLU	107	-8.428	10.140	32.379	1.00	33.36	FKBP
	ATOM	1018	OE1	GLU	107	-9.439	9.461	32.672	1.00	26.99	FKBP
	ATOM	1019	OE2	GLU	107	-8.433	11.070	31.534	1.00	36.01	FKBP
	ATOM	1020	C	GLU	107	-4.122	9.520	31.789	1.00	32.85	FKBP
	ATOM	1021	O	GLU	107	-2.875	9.520	31.888	1.00	37.58	FKBP
10	ATOM	1022	OT	GLU	107	-4.739	10.301	31.034	1.00	39.52	FKBP
	ATOM	1023	O1	RAPX	108	-7.715	26.739	39.504	1.00	6.16	RAPX
	ATOM	1024	C1	RAPX	108	-6.816	26.014	40.365	1.00	5.94	RAPX
	ATOM	1025	O2	RAPX	108	-5.659	25.863	39.953	1.00	4.69	RAPX
	ATOM	1026	C2	RAPX	108	-7.234	25.472	41.742	1.00	2.10	RAPX
15	ATOM	1027	C3	RAPX	108	-6.748	24.038	41.963	1.00	2.00	RAPX
	ATOM	1028	C4	RAPX	108	-7.531	22.968	41.204	1.00	2.86	RAPX
	ATOM	1029	C5	RAPX	108	-9.027	23.085	41.430	1.00	2.00	RAPX
	ATOM	1030	C6	RAPX	108	-9.492	24.485	41.139	1.00	2.08	RAPX
	ATOM	1031	N7	RAPX	108	-8.685	25.389	41.985	1.00	3.45	RAPX
20	ATOM	1032	C8	RAPX	108	-9.287	26.223	42.852	1.00	2.80	RAPX
	ATOM	1033	O3	RAPX	108	-8.653	27.066	43.484	1.00	4.16	RAPX
	ATOM	1034	C9	RAPX	108	-10.645	26.309	43.120	1.00	3.33	RAPX
	ATOM	1035	O4	RAPX	108	-11.026	25.607	44.055	1.00	2.89	RAPX
	ATOM	1036	C10	RAPX	108	-11.647	27.189	42.361	1.00	7.35	RAPX
25	ATOM	1037	C11	RAPX	108	-11.102	28.623	42.177	1.00	5.50	RAPX
	ATOM	1038	C12	RAPX	108	-12.102	29.453	41.362	1.00	2.25	RAPX
	ATOM	1039	C13	RAPX	108	-12.661	28.755	40.117	1.00	3.81	RAPX
	ATOM	1040	C14	RAPX	108	-12.744	27.225	40.197	1.00	5.55	RAPX
	ATOM	1041	O5	RAPX	108	-11.749	26.675	41.029	1.00	5.80	RAPX
30	ATOM	1042	O6	RAPX	108	-12.815	27.195	43.206	1.00	7.04	RAPX
	ATOM	1043	C43	RAPX	108	-10.856	29.287	43.527	1.00	10.83	RAPX
	ATOM	1044	C15	RAPX	108	-12.476	26.558	38.844	1.00	6.36	RAPX
	ATOM	1045	C16	RAPX	108	-13.491	26.688	37.700	1.00	7.22	RAPX
	ATOM	1046	O7	RAPX	108	-14.764	26.288	38.070	1.00	6.77	RAPX
35	ATOM	1047	C50	RAPX	108	-15.819	26.946	37.457	1.00	2.69	RAPX
	ATOM	1048	C17	RAPX	108	-13.020	25.794	36.553	1.00	7.17	RAPX
	ATOM	1049	C44	RAPX	108	-12.882	24.304	36.817	1.00	5.39	RAPX
	ATOM	1050	C18	RAPX	108	-12.702	26.344	35.400	1.00	12.19	RAPX
	ATOM	1051	C19	RAPX	108	-12.183	25.694	34.165	1.00	14.38	RAPX

	ATOM	1052	C20	RAPX	108	-12.264	26.351	33.003	1.00	13.32	RAPX
	ATOM	1053	C21	RAPX	108	-11.719	25.829	31.760	1.00	10.57	RAPX
	ATOM	1054	C22	RAPX	108	-10.967	26.472	30.890	1.00	7.17	RAPX
	ATOM	1055	C23	RAPX	108	-10.527	25.696	29.671	1.00	3.85	RAPX
	ATOM	1056	C45	RAPX	108	-11.166	26.303	28.459	1.00	2.00	RAPX
	ATOM	1057	C24	RAPX	108	-9.009	25.760	29.546	1.00	5.00	RAPX
	ATOM	1058	C25	RAPX	108	-8.217	25.354	30.783	1.00	6.28	RAPX
	ATOM	1059	C46	RAPX	108	-8.066	23.836	30.825	1.00	4.71	RAPX
	ATOM	1060	C26	RAPX	108	-6.853	26.023	30.751	1.00	9.09	RAPX
	ATOM	1061	O8	RAPX	108	-5.913	25.475	30.185	1.00	17.77	RAPX
	ATOM	1062	C27	RAPX	108	-6.684	27.414	31.356	1.00	14.08	RAPX
	ATOM	1063	O9	RAPX	108	-5.514	27.884	30.789	1.00	14.20	RAPX
	ATOM	1064	C51	RAPX	108	-5.711	28.919	29.903	1.00	21.98	RAPX
	ATOM	1065	C28	RAPX	108	-6.426	27.335	32.858	1.00	13.28	RAPX
	ATOM	1066	O10	RAPX	108	-5.394	26.369	33.097	1.00	17.10	RAPX
	ATOM	1067	C29	RAPX	108	-7.657	26.973	33.703	1.00	7.79	RAPX
	ATOM	1068	C47	RAPX	108	-8.663	28.083	33.806	1.00	2.00	RAPX
	ATOM	1069	C30	RAPX	108	-7.814	25.804	34.281	1.00	5.36	RAPX
	ATOM	1070	C31	RAPX	108	-8.914	25.353	35.171	1.00	5.26	RAPX
	ATOM	1071	C48	RAPX	108	-9.109	23.870	34.864	1.00	3.40	RAPX
	ATOM	1072	C32	RAPX	108	-8.560	25.557	36.644	1.00	8.61	RAPX
	ATOM	1073	O11	RAPX	108	-8.235	24.591	37.334	1.00	12.38	RAPX
	ATOM	1074	C33	RAPX	108	-8.639	26.961	37.262	1.00	6.28	RAPX
	ATOM	1075	C34	RAPX	108	-7.455	27.273	38.205	1.00	7.20	RAPX
	ATOM	1076	C35	RAPX	108	-7.353	28.808	38.512	1.00	4.56	RAPX
	ATOM	1077	C49	RAPX	108	-8.736	29.425	38.657	1.00	2.00	RAPX
	ATOM	1078	C36	RAPX	108	-6.618	29.542	37.393	1.00	6.95	RAPX
	ATOM	1079	C37	RAPX	108	-5.242	29.057	36.926	1.00	11.47	RAPX
	ATOM	1080	C38	RAPX	108	-4.839	29.836	35.667	1.00	9.55	RAPX
	ATOM	1081	C39	RAPX	108	-3.488	29.508	35.015	1.00	14.00	RAPX
	ATOM	1082	O12	RAPX	108	-3.117	30.527	34.126	1.00	21.91	RAPX
	ATOM	1083	C52	RAPX	108	-4.002	31.014	33.140	1.00	21.11	RAPX
	ATOM	1084	C40	RAPX	108	-2.354	29.491	36.072	1.00	15.37	RAPX
	ATOM	1085	O13	RAPX	108	-1.167	28.920	35.507	1.00	6.26	RAPX
	ATOM	1086	C41	RAPX	108	-2.766	28.682	37.309	1.00	13.80	RAPX
	ATOM	1087	C42	RAPX	108	-4.078	29.130	37.914	1.00	9.01	RAPX
	ATOM	1088	H6	RAPX	108	-12.593	27.124	44.143	0.00	0.00	RAPX
	ATOM	1089	H10	RAPX	108	-4.969	26.537	33.948	0.00	0.00	RAPX
	ATOM	1090	H13	RAPX	108	-0.427	29.516	35.649	0.00	0.00	RAPX

ATOM	1091	CB	ARG	2018	-17.032	35.522	6.831	1.00	40.78	FRAP
ATOM	1092	CG	ARG	2018	-18.205	36.058	7.690	1.00	39.26	FRAP
ATOM	1093	CD	ARG	2018	-18.451	35.201	8.947	1.00	39.90	FRAP
ATOM	1094	NE	ARG	2018	-17.238	35.062	9.755	1.00	40.36	FRAP
ATOM	1095	HE	ARG	2018	-16.986	35.810	10.336	0.00	0.00	FRAP
ATOM	1096	CZ	ARG	2018	-16.466	33.977	9.783	1.00	36.06	FRAP
ATOM	1097	NH1	ARG	2018	-15.238	34.057	10.282	1.00	33.73	FRAP
ATOM	1098	HH11	ARG	2018	-14.887	34.922	10.634	0.00	0.00	FRAP
ATOM	1099	HH12	ARG	2018	-14.676	33.233	10.320	0.00	0.00	FRAP
ATOM	1100	NH2	ARG	2018	-16.931	32.806	9.364	1.00	32.42	FRAP
ATOM	1101	HH21	ARG	2018	-17.868	32.729	9.020	0.00	0.00	FRAP
ATOM	1102	HH22	ARG	2018	-16.342	31.999	9.380	0.00	0.00	FRAP
ATOM	1103	C	ARG	2018	-14.580	34.887	6.780	1.00	38.22	FRAP
ATOM	1104	O	ARG	2018	-13.857	35.228	5.840	1.00	36.64	FRAP
ATOM	1105	HT1	ARG	2018	-15.235	37.392	6.027	0.00	0.00	FRAP
ATOM	1106	HT2	ARG	2018	-14.365	37.551	7.457	0.00	0.00	FRAP
ATOM	1107	N	ARG	2018	-15.291	37.286	7.064	1.00	42.10	FRAP
ATOM	1108	HT3	ARG	2018	-16.030	37.925	7.426	0.00	0.00	FRAP
ATOM	1109	CA	ARG	2018	-15.622	35.859	7.359	1.00	39.30	FRAP
ATOM	1110	N	VAL	2019	-14.474	33.705	7.388	1.00	36.94	FRAP
ATOM	1111	H	VAL	2019	-15.146	33.399	8.027	0.00	0.00	FRAP
ATOM	1112	CA	VAL	2019	-13.432	32.725	7.052	1.00	30.21	FRAP
ATOM	1113	CB	VAL	2019	-12.157	32.939	7.942	1.00	32.18	FRAP
ATOM	1114	CG1	VAL	2019	-12.536	32.966	9.417	1.00	26.50	FRAP
ATOM	1115	CG2	VAL	2019	-11.107	31.853	7.679	1.00	32.10	FRAP
ATOM	1116	C	VAL	2019	-13.973	31.314	7.273	1.00	24.65	FRAP
ATOM	1117	O	VAL	2019	-14.934	31.123	8.016	1.00	24.40	FRAP
ATOM	1118	N	ALA	2020	-13.355	30.329	6.635	1.00	22.00	FRAP
ATOM	1119	H	ALA	2020	-12.627	30.546	6.016	0.00	0.00	FRAP
ATOM	1120	CA	ALA	2020	-13.693	28.930	6.883	1.00	22.59	FRAP
ATOM	1121	CB	ALA	2020	-13.356	28.087	5.664	1.00	21.75	FRAP
ATOM	1122	C	ALA	2020	-13.000	28.354	8.125	1.00	22.82	FRAP
ATOM	1123	O	ALA	2020	-11.764	28.295	8.199	1.00	19.38	FRAP
ATOM	1124	N	ILE	2021	-13.805	27.988	9.118	1.00	20.69	FRAP
ATOM	1125	H	ILE	2021	-14.741	28.270	9.101	0.00	0.00	FRAP
ATOM	1126	CA	ILE	2021	-13.312	27.233	10.266	1.00	18.46	FRAP
ATOM	1127	CB	ILE	2021	-12.730	28.173	11.358	1.00	22.76	FRAP
ATOM	1128	CG2	ILE	2021	-13.769	29.208	11.775	1.00	25.54	FRAP
ATOM	1129	CG1	ILE	2021	-12.249	27.351	12.562	1.00	25.06	FRAP

ATOM	1130	CD1	ILE	2021	-11.140	28.005	13.366	1.00	25.45	FRAP
ATOM	1131	C	ILE	2021	-14.413	26.367	10.876	1.00	15.19	FRAP
ATOM	1132	O	ILE	2021	-15.580	26.750	10.885	1.00	15.20	FRAP
ATOM	1133	N	LEU	2022	-14.051	25.164	11.303	1.00	12.39	FRAP
ATOM	1134	H	LEU	2022	-13.191	24.841	10.981	0.00	0.00	FRAP
ATOM	1135	CA	LEU	2022	-14.967	24.324	12.072	1.00	10.94	FRAP
ATOM	1136	CB	LEU	2022	-14.339	22.958	12.314	1.00	4.40	FRAP
ATOM	1137	CG	LEU	2022	-14.001	22.196	11.041	1.00	3.20	FRAP
ATOM	1138	CD1	LEU	2022	-13.224	20.961	11.400	1.00	2.00	FRAP
ATOM	1139	CD2	LEU	2022	-15.279	21.845	10.295	1.00	2.00	FRAP
ATOM	1140	C	LEU	2022	-15.347	24.946	13.414	1.00	11.66	FRAP
ATOM	1141	O	LEU	2022	-14.489	25.468	14.134	1.00	11.57	FRAP
ATOM	1142	N	TRP	2023	-16.628	24.838	13.766	1.00	11.70	FRAP
ATOM	1143	H	TRP	2023	-17.279	24.666	13.058	0.00	0.00	FRAP
ATOM	1144	CA	TRP	2023	-17.128	25.262	15.079	1.00	13.42	FRAP
ATOM	1145	CB	TRP	2023	-18.624	24.943	15.192	1.00	6.83	FRAP
ATOM	1146	CG	TRP	2023	-19.499	25.971	14.562	1.00	2.00	FRAP
ATOM	1147	CD2	TRP	2023	-20.927	26.075	14.671	1.00	2.00	FRAP
ATOM	1148	CE2	TRP	2023	-21.309	27.257	14.015	1.00	2.00	FRAP
ATOM	1149	CE3	TRP	2023	-21.917	25.288	15.267	1.00	2.00	FRAP
ATOM	1150	CD1	TRP	2023	-19.093	27.063	13.854	1.00	2.00	FRAP
ATOM	1151	NE1	TRP	2023	-20.169	27.839	13.525	1.00	2.00	FRAP
ATOM	1152	HE1	TRP	2023	-20.112	28.705	13.064	0.00	0.00	FRAP
ATOM	1153	CZ2	TRP	2023	-22.640	27.672	13.937	1.00	2.00	FRAP
ATOM	1154	CZ3	TRP	2023	-23.241	25.706	15.188	1.00	2.00	FRAP
ATOM	1155	CH2	TRP	2023	-23.585	26.881	14.528	1.00	2.00	FRAP
ATOM	1156	C	TRP	2023	-16.359	24.603	16.230	1.00	14.99	FRAP
ATOM	1157	O	TRP	2023	-16.174	25.189	17.292	1.00	20.57	FRAP
ATOM	1158	N	HIS	2024	-15.921	23.373	15.999	1.00	17.48	FRAP
ATOM	1159	H	HIS	2024	-16.377	22.943	15.254	0.00	0.00	FRAP
ATOM	1160	CA	HIS	2024	-14.969	22.689	16.871	1.00	19.39	FRAP
ATOM	1161	CB	HIS	2024	-14.560	21.346	16.234	1.00	25.50	FRAP
ATOM	1162	CG	HIS	2024	-15.693	20.627	15.555	1.00	33.39	FRAP
ATOM	1163	CD2	HIS	2024	-16.181	20.726	14.293	1.00	33.72	FRAP
ATOM	1164	ND1	HIS	2024	-16.571	19.807	16.233	1.00	41.22	FRAP
ATOM	1165	HD1	HIS	2024	-16.490	19.465	17.152	0.00	0.00	FRAP
ATOM	1166	CE1	HIS	2024	-17.559	19.450	15.429	1.00	38.35	FRAP
ATOM	1167	NE2	HIS	2024	-17.347	19.999	14.248	1.00	38.10	FRAP
ATOM	1168	HE2	HIS	2024	-17.975	19.937	13.490	0.00	0.00	FRAP

	ATOM	1169	C	HIS	2024	-13.728	23.558	17.158	1.00	19.84	FRAP
	ATOM	1170	O	HIS	2024	-13.541	24.012	18.280	1.00	22.62	FRAP
	ATOM	1171	N	GLU	2025	-12.963	23.906	16.127	1.00	20.21	FRAP
	ATOM	1172	H	GLU	2025	-13.279	23.712	15.223	0.00	0.00	FRAP
5	ATOM	1173	CA	GLU	2025	-11.732	24.686	16.318	1.00	20.43	FRAP
	ATOM	1174	CB	GLU	2025	-10.969	24.846	14.994	1.00	27.02	FRAP
	ATOM	1175	CG	GLU	2025	-10.961	23.614	14.089	1.00	41.60	FRAP
	ATOM	1176	CD	GLU	2025	-10.550	23.937	12.652	1.00	47.27	FRAP
	ATOM	1177	OE1	GLU	2025	-9.330	23.903	12.369	1.00	54.42	FRAP
10	ATOM	1178	OE2	GLU	2025	-11.440	24.219	11.810	1.00	37.45	FRAP
	ATOM	1179	C	GLU	2025	-12.037	26.074	16.875	1.00	17.30	FRAP
	ATOM	1180	O	GLU	2025	-11.268	26.641	17.651	1.00	15.80	FRAP
	ATOM	1181	N	MET	2026	-13.159	26.625	16.444	1.00	15.93	FRAP
	ATOM	1182	H	MET	2026	-13.715	26.119	15.820	0.00	0.00	FRAP
15	ATOM	1183	CA	MET	2026	-13.552	27.971	16.816	1.00	18.01	FRAP
	ATOM	1184	CB	MET	2026	-14.806	28.354	16.021	1.00	21.46	FRAP
	ATOM	1185	CG	MET	2026	-15.619	29.490	16.603	1.00	28.72	FRAP
	ATOM	1186	SD	MET	2026	-16.931	30.032	15.505	1.00	34.40	FRAP
	ATOM	1187	CE	MET	2026	-15.938	30.642	14.095	1.00	36.70	FRAP
20	ATOM	1188	C	MET	2026	-13.805	28.060	18.325	1.00	18.72	FRAP
	ATOM	1189	O	MET	2026	-13.257	28.927	19.012	1.00	18.88	FRAP
	ATOM	1190	N	TRP	2027	-14.553	27.092	18.845	1.00	18.28	FRAP
	ATOM	1191	H	TRP	2027	-14.929	26.414	18.243	0.00	0.00	FRAP
	ATOM	1192	CA	TRP	2027	-14.890	27.047	20.263	1.00	16.52	FRAP
25	ATOM	1193	CB	TRP	2027	-16.087	26.129	20.481	1.00	14.68	FRAP
	ATOM	1194	CG	TRP	2027	-17.381	26.861	20.453	1.00	16.26	FRAP
	ATOM	1195	CD2	TRP	2027	-17.870	27.760	21.450	1.00	16.49	FRAP
	ATOM	1196	CE2	TRP	2027	-19.120	28.239	21.003	1.00	15.26	FRAP
	ATOM	1197	CE3	TRP	2027	-17.373	28.214	22.681	1.00	18.70	FRAP
30	ATOM	1198	CD1	TRP	2027	-18.322	26.831	19.466	1.00	16.17	FRAP
	ATOM	1199	NE1	TRP	2027	-19.370	27.656	19.789	1.00	13.89	FRAP
	ATOM	1200	HE1	TRP	2027	-20.150	27.816	19.215	0.00	0.00	FRAP
	ATOM	1201	CZ2	TRP	2027	-19.886	29.142	21.745	1.00	17.88	FRAP
	ATOM	1202	CZ3	TRP	2027	-18.133	29.114	23.421	1.00	17.25	FRAP
35	ATOM	1203	CH2	TRP	2027	-19.376	29.565	22.950	1.00	21.47	FRAP
	ATOM	1204	C	TRP	2027	-13.736	26.609	21.159	1.00	15.61	FRAP
	ATOM	1205	O	TRP	2027	-13.561	27.129	22.254	1.00	18.72	FRAP
	ATOM	1206	N	HIS	2028	-12.906	25.702	20.665	1.00	11.04	FRAP
	ATOM	1207	H	HIS	2028	-13.152	25.290	19.807	0.00	0.00	FRAP

	ATOM	1208	CA	HIS	2028	-11.735	25.275	21.412	1.00	10.15	FRAP
	ATOM	1209	CB	HIS	2028	-10.920	24.282	20.604	1.00	9.23	FRAP
	ATOM	1210	CG	HIS	2028	-9.821	23.642	21.389	1.00	10.39	FRAP
	ATOM	1211	CD2	HIS	2028	-9.786	22.484	22.091	1.00	8.51	FRAP
5	ATOM	1212	ND1	HIS	2028	-8.575	24.215	21.529	1.00	13.26	FRAP
	ATOM	1213	HD1	HIS	2028	-8.284	25.084	21.180	0.00	0.00	FRAP
	ATOM	1214	CE1	HIS	2028	-7.814	23.433	22.276	1.00	15.69	FRAP
	ATOM	1215	NE2	HIS	2028	-8.527	22.377	22.629	1.00	18.29	FRAP
	ATOM	1216	HE2	HIS	2028	-8.221	21.579	23.119	0.00	0.00	FRAP
10	ATOM	1217	C	HIS	2028	-10.827	26.424	21.805	1.00	10.27	FRAP
	ATOM	1218	O	HIS	2028	-10.401	26.519	22.941	1.00	10.19	FRAP
	ATOM	1219	N	GLU	2029	-10.360	27.167	20.817	1.00	19.72	FRAP
	ATOM	1220	H	GLU	2029	-10.688	27.017	19.900	0.00	0.00	FRAP
	ATOM	1221	CA	GLU	2029	-9.433	28.257	21.093	1.00	27.56	FRAP
15	ATOM	1222	CB	GLU	2029	-8.601	28.592	19.843	1.00	34.06	FRAP
	ATOM	1223	CG	GLU	2029	-9.401	28.822	18.565	1.00	44.39	FRAP
	ATOM	1224	CD	GLU	2029	-8.554	28.678	17.307	1.00	50.63	FRAP
	ATOM	1225	OE1	GLU	2029	-8.624	29.570	16.429	1.00	54.55	FRAP
	ATOM	1226	OE2	GLU	2029	-7.828	27.664	17.191	1.00	51.32	FRAP
20	ATOM	1227	C	GLU	2029	-10.133	29.508	21.642	1.00	27.45	FRAP
	ATOM	1228	O	GLU	2029	-9.533	30.277	22.392	1.00	29.68	FRAP
	ATOM	1229	N	GLY	2030	-11.433	29.634	21.380	1.00	25.66	FRAP
	ATOM	1230	H	GLY	2030	-11.843	29.093	20.670	0.00	0.00	FRAP
	ATOM	1231	CA	GLY	2030	-12.214	30.696	21.997	1.00	21.35	FRAP
25	ATOM	1232	C	GLY	2030	-12.307	30.538	23.504	1.00	16.02	FRAP
	ATOM	1233	O	GLY	2030	-11.837	31.390	24.257	1.00	17.01	FRAP
	ATOM	1234	N	LEU	2031	-12.767	29.368	23.932	1.00	11.25	FRAP
	ATOM	1235	H	LEU	2031	-13.130	28.749	23.264	0.00	0.00	FRAP
	ATOM	1236	CA	LEU	2031	-12.805	29.012	25.341	1.00	6.54	FRAP
30	ATOM	1237	CB	LEU	2031	-13.382	27.612	25.511	1.00	2.00	FRAP
	ATOM	1238	CG	LEU	2031	-14.869	27.475	25.192	1.00	2.25	FRAP
	ATOM	1239	CD1	LEU	2031	-15.347	26.079	25.568	1.00	2.00	FRAP
	ATOM	1240	CD2	LEU	2031	-15.656	28.530	25.936	1.00	2.00	FRAP
	ATOM	1241	C	LEU	2031	-11.441	29.088	26.024	1.00	10.09	FRAP
35	ATOM	1242	O	LEU	2031	-11.337	29.538	27.168	1.00	16.95	FRAP
	ATOM	1243	N	GLU	2032	-10.386	28.657	25.348	1.00	8.34	FRAP
	ATOM	1244	H	GLU	2032	-10.522	28.216	24.483	0.00	0.00	FRAP
	ATOM	1245	CA	GLU	2032	-9.068	28.756	25.957	1.00	12.37	FRAP
	ATOM	1246	CB	GLU	2032	-8.028	27.986	25.146	1.00	16.26	FRAP

ATOM	1247	CG	GLU	2032	-6.692	27.831	25.861	1.00	23.62	FRAP
ATOM	1248	CD	GLU	2032	-5.792	26.772	25.235	1.00	30.03	FRAP
ATOM	1249	OE1	GLU	2032	-4.617	27.092	24.948	1.00	31.98	FRAP
ATOM	1250	OE2	GLU	2032	-6.241	25.611	25.078	1.00	32.01	FRAP
ATOM	1251	C	GLU	2032	-8.629	30.210	26.154	1.00	12.81	FRAP
ATOM	1252	O	GLU	2032	-8.263	30.588	27.261	1.00	21.81	FRAP
ATOM	1253	N	GLU	2033	-8.837	31.053	25.147	1.00	11.47	FRAP
ATOM	1254	H	GLU	2033	-9.243	30.710	24.323	0.00	0.00	FRAP
ATOM	1255	CA	GLU	2033	-8.462	32.473	25.225	1.00	12.69	FRAP
ATOM	1256	CB	GLU	2033	-8.631	33.140	23.854	1.00	19.44	FRAP
ATOM	1257	CG	GLU	2033	-7.834	34.437	23.650	1.00	30.82	FRAP
ATOM	1258	CD	GLU	2033	-8.155	35.152	22.319	1.00	42.12	FRAP
ATOM	1259	OE1	GLU	2033	-7.793	36.346	22.186	1.00	44.44	FRAP
ATOM	1260	OE2	GLU	2033	-8.759	34.530	21.408	1.00	39.63	FRAP
ATOM	1261	C	GLU	2033	-9.308	33.226	26.254	1.00	10.31	FRAP
ATOM	1262	O	GLU	2033	-8.808	34.068	26.994	1.00	6.92	FRAP
ATOM	1263	N	ALA	2034	-10.600	32.933	26.275	1.00	6.18	FRAP
ATOM	1264	H	ALA	2034	-10.945	32.334	25.587	0.00	0.00	FRAP
ATOM	1265	CA	ALA	2034	-11.509	33.572	27.205	1.00	2.76	FRAP
ATOM	1266	CB	ALA	2034	-12.920	33.101	26.943	1.00	2.50	FRAP
ATOM	1267	C	ALA	2034	-11.101	33.257	28.641	1.00	6.07	FRAP
ATOM	1268	O	ALA	2034	-10.907	34.157	29.453	1.00	11.33	FRAP
ATOM	1269	N	SER	2035	-10.811	31.988	28.903	1.00	8.47	FRAP
ATOM	1270	H	SER	2035	-10.871	31.330	28.175	0.00	0.00	FRAP
ATOM	1271	CA	SER	2035	-10.482	31.543	30.250	1.00	4.56	FRAP
ATOM	1272	CB	SER	2035	-10.357	30.016	30.294	1.00	2.00	FRAP
ATOM	1273	OG	SER	2035	-9.012	29.595	30.200	1.00	7.26	FRAP
ATOM	1274	HG	SER	2035	-8.700	29.696	29.288	0.00	0.00	FRAP
ATOM	1275	C	SER	2035	-9.201	32.193	30.749	1.00	5.40	FRAP
ATOM	1276	O	SER	2035	-9.171	32.734	31.846	1.00	11.51	FRAP
ATOM	1277	N	ARG	2036	-8.195	32.265	29.886	1.00	3.96	FRAP
ATOM	1278	H	ARG	2036	-8.314	31.862	28.998	0.00	0.00	FRAP
ATOM	1279	CA	ARG	2036	-6.934	32.909	30.233	1.00	6.68	FRAP
ATOM	1280	CB	ARG	2036	-5.959	32.792	29.065	1.00	7.24	FRAP
ATOM	1281	CG	ARG	2036	-4.695	33.631	29.210	1.00	17.54	FRAP
ATOM	1282	CD	ARG	2036	-4.229	34.185	27.860	1.00	17.93	FRAP
ATOM	1283	NE	ARG	2036	-3.637	35.515	27.997	1.00	18.57	FRAP
ATOM	1284	HE	ARG	2036	-2.897	35.626	28.628	0.00	0.00	FRAP
ATOM	1285	CZ	ARG	2036	-4.055	36.595	27.344	1.00	20.32	FRAP

ATOM	1286	NH1	ARG	2036	-3.456	37.762	27.540	1.00	24.32	FRAP
ATOM	1287	HH11	ARG	2036	-2.689	37.827	28.180	0.00	0.00	FRAP
ATOM	1288	HH12	ARG	2036	-3.766	38.572	27.045	0.00	0.00	FRAP
ATOM	1289	NH2	ARG	2036	-5.080	36.518	26.505	1.00	20.76	FRAP
ATOM	1290	HH21	ARG	2036	-5.564	35.653	26.375	0.00	0.00	FRAP
ATOM	1291	HH22	ARG	2036	-5.391	37.341	26.030	0.00	0.00	FRAP
ATOM	1292	C	ARG	2036	-7.110	34.382	30.624	1.00	9.31	FRAP
ATOM	1293	O	ARG	2036	-6.463	34.872	31.548	1.00	12.91	FRAP
ATOM	1294	N	LEU	2037	-8.041	35.057	29.964	1.00	10.78	FRAP
ATOM	1295	H	LEU	2037	-8.541	34.590	29.261	0.00	0.00	FRAP
ATOM	1296	CA	LEU	2037	-8.309	36.466	30.214	1.00	8.83	FRAP
ATOM	1297	CB	LEU	2037	-9.163	37.034	29.084	1.00	9.75	FRAP
ATOM	1298	CG	LEU	2037	-8.302	37.375	27.873	1.00	8.95	FRAP
ATOM	1299	CD1	LEU	2037	-9.130	37.388	26.613	1.00	11.32	FRAP
ATOM	1300	CD2	LEU	2037	-7.624	38.713	28.110	1.00	7.83	FRAP
ATOM	1301	C	LEU	2037	-9.004	36.692	31.543	1.00	12.66	FRAP
ATOM	1302	O	LEU	2037	-8.626	37.583	32.295	1.00	17.85	FRAP
ATOM	1303	N	TYR	2038	-10.020	35.886	31.832	1.00	11.90	FRAP
ATOM	1304	H	TYR	2038	-10.327	35.266	31.130	0.00	0.00	FRAP
ATOM	1305	CA	TYR	2038	-10.693	35.930	33.132	1.00	11.68	FRAP
ATOM	1306	CB	TYR	2038	-12.006	35.138	33.071	1.00	9.29	FRAP
ATOM	1307	CG	TYR	2038	-12.761	35.090	34.375	1.00	12.17	FRAP
ATOM	1308	CD1	TYR	2038	-12.942	36.239	35.143	1.00	10.58	FRAP
ATOM	1309	CE1	TYR	2038	-13.555	36.181	36.391	1.00	17.63	FRAP
ATOM	1310	CD2	TYR	2038	-13.230	33.880	34.884	1.00	17.46	FRAP
ATOM	1311	CE2	TYR	2038	-13.850	33.810	36.131	1.00	17.47	FRAP
ATOM	1312	CZ	TYR	2038	-14.006	34.962	36.880	1.00	18.99	FRAP
ATOM	1313	OH	TYR	2038	-14.596	34.893	38.123	1.00	22.39	FRAP
ATOM	1314	HH	TYR	2038	-15.321	34.267	38.078	0.00	0.00	FRAP
ATOM	1315	C	TYR	2038	-9.811	35.403	34.277	1.00	13.86	FRAP
ATOM	1316	O	TYR	2038	-9.408	36.164	35.158	1.00	17.65	FRAP
ATOM	1317	N	PHE	2039	-9.481	34.113	34.235	1.00	13.85	FRAP
ATOM	1318	H	PHE	2039	-9.764	33.595	33.452	0.00	0.00	FRAP
ATOM	1319	CA	PHE	2039	-8.717	33.455	35.299	1.00	10.83	FRAP
ATOM	1320	CB	PHE	2039	-8.665	31.950	35.054	1.00	2.58	FRAP
ATOM	1321	CG	PHE	2039	-9.988	31.281	35.235	1.00	6.64	FRAP
ATOM	1322	CD1	PHE	2039	-10.540	31.147	36.510	1.00	4.84	FRAP
ATOM	1323	CD2	PHE	2039	-10.745	30.902	34.131	1.00	2.79	FRAP
ATOM	1324	CE1	PHE	2039	-11.828	30.656	36.680	1.00	5.26	FRAP

ATOM	1325	CE2	PHE	2039	-12.039	30.408	34.292	1.00	2.18	FRAP
ATOM	1326	CZ	PHE	2039	-12.581	30.287	35.563	1.00	4.94	FRAP
ATOM	1327	C	PHE	2039	-7.306	33.980	35.460	1.00	14.37	FRAP
ATOM	1328	O	PHE	2039	-6.861	34.248	36.579	1.00	15.23	FRAP
ATOM	1329	N	GLY	2040	-6.619	34.155	34.336	1.00	17.70	FRAP
ATOM	1330	H	GLY	2040	-7.060	34.013	33.471	0.00	0.00	FRAP
ATOM	1331	CA	GLY	2040	-5.221	34.544	34.369	1.00	19.07	FRAP
ATOM	1332	C	GLY	2040	-4.954	36.026	34.561	1.00	19.43	FRAP
ATOM	1333	O	GLY	2040	-3.957	36.384	35.180	1.00	24.65	FRAP
ATOM	1334	N	GLU	2041	-5.815	36.881	34.012	1.00	17.18	FRAP
ATOM	1335	H	GLU	2041	-6.555	36.502	33.494	0.00	0.00	FRAP
ATOM	1336	CA	GLU	2041	-5.590	38.328	34.019	1.00	16.74	FRAP
ATOM	1337	CB	GLU	2041	-5.476	38.867	32.589	1.00	21.26	FRAP
ATOM	1338	CG	GLU	2041	-5.030	37.856	31.544	1.00	34.57	FRAP
ATOM	1339	CD	GLU	2041	-3.792	38.302	30.785	1.00	39.88	FRAP
ATOM	1340	OE1	GLU	2041	-3.772	39.459	30.303	1.00	41.61	FRAP
ATOM	1341	OE2	GLU	2041	-2.844	37.489	30.664	1.00	43.16	FRAP
ATOM	1342	C	GLU	2041	-6.689	39.108	34.733	1.00	16.00	FRAP
ATOM	1343	O	GLU	2041	-6.754	40.330	34.629	1.00	16.19	FRAP
ATOM	1344	N	ARG	2042	-7.626	38.392	35.340	1.00	16.54	FRAP
ATOM	1345	H	ARG	2042	-7.540	37.419	35.364	0.00	0.00	FRAP
ATOM	1346	CA	ARG	2042	-8.785	39.011	35.974	1.00	17.30	FRAP
ATOM	1347	CB	ARG	2042	-8.389	39.691	37.283	1.00	21.74	FRAP
ATOM	1348	CG	ARG	2042	-8.704	38.869	38.515	1.00	29.43	FRAP
ATOM	1349	CD	ARG	2042	-7.650	37.815	38.736	1.00	31.60	FRAP
ATOM	1350	NE	ARG	2042	-6.318	38.396	38.627	1.00	34.93	FRAP
ATOM	1351	HE	ARG	2042	-6.148	39.074	37.940	0.00	0.00	FRAP
ATOM	1352	CZ	ARG	2042	-5.273	38.026	39.358	1.00	41.93	FRAP
ATOM	1353	NH1	ARG	2042	-4.097	38.606	39.146	1.00	43.89	FRAP
ATOM	1354	HH11	ARG	2042	-4.011	39.312	38.444	0.00	0.00	FRAP
ATOM	1355	HH12	ARG	2042	-3.309	38.359	39.710	0.00	0.00	FRAP
ATOM	1356	NH2	ARG	2042	-5.398	37.089	40.296	1.00	42.95	FRAP
ATOM	1357	HH21	ARG	2042	-6.289	36.673	40.485	0.00	0.00	FRAP
ATOM	1358	HH22	ARG	2042	-4.609	36.857	40.865	0.00	0.00	FRAP
ATOM	1359	C	ARG	2042	-9.485	40.015	35.074	1.00	15.46	FRAP
ATOM	1360	O	ARG	2042	-10.031	41.009	35.550	1.00	17.81	FRAP
ATOM	1361	N	ASN	2043	-9.560	39.689	33.789	1.00	13.57	FRAP
ATOM	1362	H	ASN	2043	-9.152	38.845	33.525	0.00	0.00	FRAP
ATOM	1363	CA	ASN	2043	-10.219	40.545	32.805	1.00	12.63	FRAP

	ATOM	1364	CB	ASN	2043	-9.322	40.702	31.567	1.00	9.40	FRAP
	ATOM	1365	CG	ASN	2043	-9.673	41.928	30.734	1.00	13.89	FRAP
	ATOM	1366	OD1	ASN	2043	-10.778	42.457	30.805	1.00	13.79	FRAP
	ATOM	1367	ND2	ASN	2043	-8.725	42.382	29.941	1.00	19.98	FRAP
	ATOM	1368	HD21	ASN	2043	-7.861	41.929	29.933	0.00	0.00	FRAP
	ATOM	1369	HD22	ASN	2043	-8.951	43.171	29.415	0.00	0.00	FRAP
	ATOM	1370	C	ASN	2043	-11.589	39.985	32.399	1.00	11.08	FRAP
	ATOM	1371	O	ASN	2043	-11.704	39.254	31.410	1.00	15.73	FRAP
	ATOM	1372	N	VAL	2044	-12.622	40.329	33.164	1.00	7.83	FRAP
	ATOM	1373	H	VAL	2044	-12.407	40.817	33.986	0.00	0.00	FRAP
	ATOM	1374	CA	VAL	2044	-13.996	39.930	32.841	1.00	8.89	FRAP
	ATOM	1375	CB	VAL	2044	-14.942	40.079	34.049	1.00	4.93	FRAP
	ATOM	1376	CG1	VAL	2044	-16.254	39.343	33.783	1.00	2.00	FRAP
	ATOM	1377	CG2	VAL	2044	-14.280	39.541	35.300	1.00	6.55	FRAP
	ATOM	1378	C	VAL	2044	-14.599	40.724	31.680	1.00	12.31	FRAP
	ATOM	1379	O	VAL	2044	-15.607	40.328	31.111	1.00	16.97	FRAP
	ATOM	1380	N	LYS	2045	-14.013	41.873	31.366	1.00	15.26	FRAP
	ATOM	1381	H	LYS	2045	-13.326	42.230	31.961	0.00	0.00	FRAP
	ATOM	1382	CA	LYS	2045	-14.387	42.614	30.158	1.00	18.66	FRAP
	ATOM	1383	CB	LYS	2045	-13.791	44.027	30.205	1.00	20.39	FRAP
	ATOM	1384	CG	LYS	2045	-13.868	44.787	28.894	1.00	27.87	FRAP
	ATOM	1385	CD	LYS	2045	-12.848	45.913	28.846	1.00	36.04	FRAP
	ATOM	1386	CE	LYS	2045	-13.013	46.763	27.592	1.00	39.79	FRAP
	ATOM	1387	NZ	LYS	2045	-12.203	48.015	27.646	1.00	42.34	FRAP
	ATOM	1388	HZ1	LYS	2045	-11.194	47.773	27.696	0.00	0.00	FRAP
	ATOM	1389	HZ2	LYS	2045	-12.477	48.555	28.491	0.00	0.00	FRAP
	ATOM	1390	HZ3	LYS	2045	-12.387	48.579	26.791	0.00	0.00	FRAP
	ATOM	1391	C	LYS	2045	-13.912	41.880	28.890	1.00	15.74	FRAP
	ATOM	1392	O	LYS	2045	-14.697	41.616	27.982	1.00	15.10	FRAP
	ATOM	1393	N	GLY	2046	-12.640	41.493	28.885	1.00	13.71	FRAP
	ATOM	1394	H	GLY	2046	-12.091	41.759	29.647	0.00	0.00	FRAP
	ATOM	1395	CA	GLY	2046	-12.063	40.767	27.768	1.00	11.16	FRAP
	ATOM	1396	C	GLY	2046	-12.716	39.427	27.486	1.00	11.68	FRAP
	ATOM	1397	O	GLY	2046	-13.079	39.138	26.350	1.00	12.25	FRAP
	ATOM	1398	N	MET	2047	-12.944	38.632	28.522	1.00	14.02	FRAP
	ATOM	1399	H	MET	2047	-12.639	38.911	29.412	0.00	0.00	FRAP
	ATOM	1400	CA	MET	2047	-13.555	37.327	28.317	1.00	12.90	FRAP
	ATOM	1401	CB	MET	2047	-13.571	36.520	29.625	1.00	9.26	FRAP
	ATOM	1402	CG	MET	2047	-14.762	36.725	30.521	1.00	6.02	FRAP

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ATOM   1403  SD  MET  2047     -15.175  35.189  31.335  1.00  6.46      FRAP
ATOM   1404  CE  MET  2047     -16.865  35.461  31.714  1.00  4.80      FRAP
ATOM   1405  C   MET  2047     -14.954  37.413  27.691  1.00 14.99      FRAP
ATOM   1406  O   MET  2047     -15.275  36.624  26.816  1.00 20.34      FRAP
ATOM   1407  N   PHE  2048     -15.710  38.465  28.001  1.00 13.61      FRAP
ATOM   1408  H   PHE  2048     -15.410  39.078  28.703  0.00  0.00      FRAP
ATOM   1409  CA  PHE  2048     -16.992  38.707  27.324  1.00 12.00      FRAP
ATOM   1410  CB  PHE  2048     -17.754  39.849  28.012  1.00 15.37      FRAP
ATOM   1411  CG  PHE  2048     -18.356  39.479  29.357  1.00 19.64      FRAP
ATOM   1412  CD1 PHE  2048     -18.849  38.201  29.600  1.00 20.36      FRAP
ATOM   1413  CD2 PHE  2048     -18.506  40.442  30.352  1.00 17.04      FRAP
ATOM   1414  CE1 PHE  2048     -19.481  37.901  30.806  1.00 12.14      FRAP
ATOM   1415  CE2 PHE  2048     -19.137  40.138  31.552  1.00  7.86      FRAP
ATOM   1416  CZ  PHE  2048     -19.623  38.875  31.774  1.00  2.66      FRAP
ATOM   1417  C   PHE  2048     -16.785  39.054  25.839  1.00 11.47      FRAP
ATOM   1418  O   PHE  2048     -17.540  38.619  24.968  1.00  9.57      FRAP
ATOM   1419  N   GLU  2049     -15.754  39.843  25.558  1.00 10.97      FRAP
ATOM   1420  H   GLU  2049     -15.274  40.244  26.315  0.00  0.00      FRAP
ATOM   1421  CA  GLU  2049     -15.368  40.161  24.189  1.00 12.08      FRAP
ATOM   1422  CB  GLU  2049     -14.144  41.090  24.187  1.00 18.49      FRAP
ATOM   1423  CG  GLU  2049     -14.432  42.512  24.700  1.00 28.61      FRAP
ATOM   1424  CD  GLU  2049     -13.244  43.464  24.566  1.00 32.92      FRAP
ATOM   1425  OE1 GLU  2049     -13.006  44.240  25.521  1.00 34.23      FRAP
ATOM   1426  OE2 GLU  2049     -12.598  43.492  23.489  1.00 32.94      FRAP
ATOM   1427  C   GLU  2049     -15.072  38.890  23.387  1.00 10.88      FRAP
ATOM   1428  O   GLU  2049     -15.771  38.579  22.427  1.00 12.08      FRAP
ATOM   1429  N   VAL  2050     -14.120  38.096  23.862  1.00 10.17      FRAP
ATOM   1430  H   VAL  2050     -13.667  38.388  24.675  0.00  0.00      FRAP
ATOM   1431  CA  VAL  2050     -13.800  36.807  23.247  1.00 10.01      FRAP
ATOM   1432  CB  VAL  2050     -12.318  36.446  23.457  1.00  6.62      FRAP
ATOM   1433  CG1 VAL  2050     -11.942  36.639  24.901  1.00 11.08      FRAP
ATOM   1434  CG2 VAL  2050     -12.039  35.006  22.995  1.00 11.04      FRAP
ATOM   1435  C   VAL  2050     -14.693  35.680  23.781  1.00 14.92      FRAP
ATOM   1436  O   VAL  2050     -14.244  34.799  24.529  1.00 20.63      FRAP
ATOM   1437  N   LEU  2051     -15.981  35.775  23.454  1.00 12.19      FRAP
ATOM   1438  H   LEU  2051     -16.263  36.655  23.111  0.00  0.00      FRAP
ATOM   1439  CA  LEU  2051     -16.971  34.764  23.816  1.00  9.54      FRAP
ATOM   1440  CB  LEU  2051     -17.122  34.686  25.336  1.00  8.37      FRAP
ATOM   1441  CG  LEU  2051     -17.216  33.329  26.046  1.00  8.86      FRAP
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ATOM	1442	CD1	LEU	2051	-16.110	32.395	25.592	1.00	5.79	FRAP
ATOM	1443	CD2	LEU	2051	-17.118	33.550	27.538	1.00	2.00	FRAP
ATOM	1444	C	LEU	2051	-18.310	35.117	23.188	1.00	10.79	FRAP
ATOM	1445	O	LEU	2051	-19.052	34.237	22.752	1.00	14.03	FRAP
ATOM	1446	N	GLU	2052	-18.562	36.413	23.042	1.00	11.63	FRAP
ATOM	1447	H	GLU	2052	-17.932	37.078	23.408	0.00	0.00	FRAP
ATOM	1448	CA	GLU	2052	-19.837	36.897	22.525	1.00	13.53	FRAP
ATOM	1449	CB	GLU	2052	-19.980	38.399	22.792	1.00	18.53	FRAP
ATOM	1450	CG	GLU	2052	-21.396	38.835	23.103	1.00	29.17	FRAP
ATOM	1451	CD	GLU	2052	-21.530	40.343	23.220	1.00	34.41	FRAP
ATOM	1452	OE1	GLU	2052	-22.567	40.884	22.772	1.00	39.61	FRAP
ATOM	1453	OE2	GLU	2052	-20.605	40.987	23.766	1.00	36.83	FRAP
ATOM	1454	C	GLU	2052	-20.059	36.587	21.044	1.00	9.88	FRAP
ATOM	1455	O	GLU	2052	-21.045	35.948	20.693	1.00	11.10	FRAP
ATOM	1456	N	PRO	2053	-19.085	36.922	20.175	1.00	9.83	FRAP
ATOM	1457	CD	PRO	2053	-18.104	38.004	20.386	1.00	7.70	FRAP
ATOM	1458	CA	PRO	2053	-18.978	36.374	18.814	1.00	9.97	FRAP
ATOM	1459	CB	PRO	2053	-17.537	36.674	18.444	1.00	12.18	FRAP
ATOM	1460	CG	PRO	2053	-17.265	37.981	19.139	1.00	11.41	FRAP
ATOM	1461	C	PRO	2053	-19.301	34.882	18.639	1.00	11.69	FRAP
ATOM	1462	O	PRO	2053	-20.157	34.520	17.837	1.00	15.54	FRAP
ATOM	1463	N	LEU	2054	-18.588	34.021	19.362	1.00	12.26	FRAP
ATOM	1464	H	LEU	2054	-17.894	34.386	19.944	0.00	0.00	FRAP
ATOM	1465	CA	LEU	2054	-18.813	32.574	19.304	1.00	7.01	FRAP
ATOM	1466	CB	LEU	2054	-17.897	31.859	20.296	1.00	2.00	FRAP
ATOM	1467	CG	LEU	2054	-16.431	32.303	20.307	1.00	2.00	FRAP
ATOM	1468	CD1	LEU	2054	-15.603	31.503	21.299	1.00	2.00	FRAP
ATOM	1469	CD2	LEU	2054	-15.873	32.146	18.921	1.00	12.00	FRAP
ATOM	1470	C	LEU	2054	-20.267	32.247	19.621	1.00	6.82	FRAP
ATOM	1471	O	LEU	2054	-20.928	31.510	18.895	1.00	7.84	FRAP
ATOM	1472	N	HIS	2055	-20.805	32.908	20.632	1.00	4.28	FRAP
ATOM	1473	H	HIS	2055	-20.241	33.532	21.142	0.00	0.00	FRAP
ATOM	1474	CA	HIS	2055	-22.205	32.716	20.965	1.00	5.58	FRAP
ATOM	1475	CB	HIS	2055	-22.533	33.366	22.310	1.00	5.95	FRAP
ATOM	1476	CG	HIS	2055	-22.237	32.495	23.491	1.00	2.00	FRAP
ATOM	1477	CD2	HIS	2055	-21.136	32.399	24.270	1.00	2.00	FRAP
ATOM	1478	ND1	HIS	2055	-23.118	31.542	23.952	1.00	2.00	FRAP
ATOM	1479	HD1	HIS	2055	-24.025	31.364	23.581	0.00	0.00	FRAP
ATOM	1480	CE1	HIS	2055	-22.569	30.891	24.960	1.00	2.00	FRAP

ATOM	1481	NE2	HIS	2055	-21.362	31.384	25.166	1.00	3.10	FRAP
ATOM	1482	HE2	HIS	2055	-20.608	30.877	25.532	0.00	0.00	FRAP
ATOM	1483	C	HIS	2055	-23.118	33.276	19.884	1.00	8.31	FRAP
ATOM	1484	O	HIS	2055	-24.215	32.765	19.667	1.00	14.91	FRAP
ATOM	1485	N	ALA	2056	-22.644	34.290	19.170	1.00	10.33	FRAP
ATOM	1486	H	ALA	2056	-21.767	34.651	19.397	0.00	0.00	FRAP
ATOM	1487	CA	ALA	2056	-23.442	34.935	18.130	1.00	10.51	FRAP
ATOM	1488	CB	ALA	2056	-22.729	36.161	17.619	1.00	9.92	FRAP
ATOM	1489	C	ALA	2056	-23.731	33.985	16.974	1.00	14.24	FRAP
ATOM	1490	O	ALA	2056	-24.885	33.829	16.556	1.00	17.21	FRAP
ATOM	1491	N	MET	2057	-22.680	33.340	16.476	1.00	11.79	FRAP
ATOM	1492	H	MET	2057	-21.792	33.596	16.814	0.00	0.00	FRAP
ATOM	1493	CA	MET	2057	-22.810	32.294	15.469	1.00	15.13	FRAP
ATOM	1494	CB	MET	2057	-21.452	31.642	15.231	1.00	17.94	FRAP
ATOM	1495	CG	MET	2057	-20.692	32.266	14.087	1.00	27.92	FRAP
ATOM	1496	SD	MET	2057	-18.979	31.767	14.037	1.00	39.79	FRAP
ATOM	1497	CE	MET	2057	-18.164	33.353	14.482	1.00	41.99	FRAP
ATOM	1498	C	MET	2057	-23.842	31.222	15.834	1.00	17.76	FRAP
ATOM	1499	O	MET	2057	-24.808	31.000	15.100	1.00	16.63	FRAP
ATOM	1500	N	MET	2058	-23.679	30.615	17.005	1.00	20.22	FRAP
ATOM	1501	H	MET	2058	-22.898	30.870	17.543	0.00	0.00	FRAP
ATOM	1502	CA	MET	2058	-24.617	29.603	17.489	1.00	21.71	FRAP
ATOM	1503	CB	MET	2058	-24.359	29.323	18.969	1.00	20.36	FRAP
ATOM	1504	CG	MET	2058	-22.991	28.760	19.256	1.00	15.47	FRAP
ATOM	1505	SD	MET	2058	-22.714	27.281	18.302	1.00	20.16	FRAP
ATOM	1506	CE	MET	2058	-23.353	26.049	19.380	1.00	12.03	FRAP
ATOM	1507	C	MET	2058	-26.074	30.032	17.295	1.00	25.10	FRAP
ATOM	1508	O	MET	2058	-26.865	29.330	16.659	1.00	28.18	FRAP
ATOM	1509	N	GLU	2059	-26.375	31.246	17.742	1.00	25.58	FRAP
ATOM	1510	H	GLU	2059	-25.654	31.794	18.125	0.00	0.00	FRAP
ATOM	1511	CA	GLU	2059	-27.725	31.798	17.694	1.00	26.53	FRAP
ATOM	1512	CB	GLU	2059	-27.759	33.099	18.504	1.00	26.67	FRAP
ATOM	1513	CG	GLU	2059	-29.007	33.941	18.330	1.00	28.36	FRAP
ATOM	1514	CD	GLU	2059	-28.701	35.344	17.828	1.00	34.40	FRAP
ATOM	1515	OE1	GLU	2059	-27.515	35.648	17.560	1.00	37.80	FRAP
ATOM	1516	OE2	GLU	2059	-29.653	36.146	17.699	1.00	36.02	FRAP
ATOM	1517	C	GLU	2059	-28.224	32.039	16.261	1.00	24.75	FRAP
ATOM	1518	O	GLU	2059	-29.425	32.148	16.022	1.00	24.66	FRAP
ATOM	1519	N	ARG	2060	-27.303	32.057	15.307	1.00	23.58	FRAP

	ATOM	1520	H	ARG	2060	-26.365	31.985	15.562	0.00	0.00	FRAP
	ATOM	1521	CA	ARG	2060	-27.660	32.296	13.914	1.00	27.89	FRAP
	ATOM	1522	CB	ARG	2060	-26.547	33.091	13.224	1.00	31.68	FRAP
	ATOM	1523	CG	ARG	2060	-26.338	34.497	13.808	1.00	33.63	FRAP
5	ATOM	1524	CD	ARG	2060	-27.275	35.527	13.173	1.00	36.15	FRAP
	ATOM	1525	NE	ARG	2060	-28.381	35.927	14.046	1.00	35.55	FRAP
	ATOM	1526	HE	ARG	2060	-28.189	36.558	14.770	0.00	0.00	FRAP
	ATOM	1527	CZ	ARG	2060	-29.635	35.492	13.924	1.00	37.00	FRAP
	ATOM	1528	NH1	ARG	2060	-30.590	35.982	14.704	1.00	38.84	FRAP
10	ATOM	1529	HH11	ARG	2060	-30.376	36.677	15.389	0.00	0.00	FRAP
	ATOM	1530	HH12	ARG	2060	-31.526	35.646	14.601	0.00	0.00	FRAP
	ATOM	1531	NH2	ARG	2060	-29.933	34.533	13.057	1.00	33.57	FRAP
	ATOM	1532	HH21	ARG	2060	-29.220	34.125	12.486	0.00	0.00	FRAP
	ATOM	1533	HH22	ARG	2060	-30.874	34.210	12.967	0.00	0.00	FRAP
15	ATOM	1534	C	ARG	2060	-27.992	31.021	13.117	1.00	26.90	FRAP
	ATOM	1535	O	ARG	2060	-28.925	31.013	12.317	1.00	26.30	FRAP
	ATOM	1536	N	GLY	2061	-27.246	29.945	13.351	1.00	27.44	FRAP
	ATOM	1537	H	GLY	2061	-26.500	30.030	13.976	0.00	0.00	FRAP
	ATOM	1538	CA	GLY	2061	-27.597	28.662	12.758	1.00	23.84	FRAP
20	ATOM	1539	C	GLY	2061	-26.442	27.751	12.361	1.00	25.08	FRAP
	ATOM	1540	O	GLY	2061	-25.500	28.198	11.690	1.00	29.79	FRAP
	ATOM	1541	N	PRO	2062	-26.516	26.448	12.695	1.00	21.10	FRAP
	ATOM	1542	CD	PRO	2062	-27.590	25.836	13.489	1.00	18.97	FRAP
	ATOM	1543	CA	PRO	2062	-25.740	25.433	11.976	1.00	19.45	FRAP
25	ATOM	1544	CB	PRO	2062	-26.204	24.110	12.585	1.00	14.25	FRAP
	ATOM	1545	CG	PRO	2062	-27.072	24.467	13.734	1.00	14.98	FRAP
	ATOM	1546	C	PRO	2062	-26.051	25.463	10.487	1.00	21.95	FRAP
	ATOM	1547	O	PRO	2062	-27.208	25.349	10.085	1.00	26.38	FRAP
	ATOM	1548	N	GLN	2063	-25.048	25.729	9.670	1.00	21.33	FRAP
30	ATOM	1549	H	GLN	2063	-24.240	26.065	10.056	0.00	0.00	FRAP
	ATOM	1550	CA	GLN	2063	-25.258	25.668	8.224	1.00	22.88	FRAP
	ATOM	1551	CB	GLN	2063	-24.384	26.700	7.510	1.00	25.75	FRAP
	ATOM	1552	CG	GLN	2063	-25.131	27.922	7.002	1.00	30.23	FRAP
	ATOM	1553	CD	GLN	2063	-24.186	29.035	6.545	1.00	37.47	FRAP
35	ATOM	1554	OE1	GLN	2063	-23.139	28.776	5.945	1.00	42.91	FRAP
	ATOM	1555	NE2	GLN	2063	-24.556	30.280	6.822	1.00	34.40	FRAP
	ATOM	1556	HE21	GLN	2063	-25.396	30.488	7.270	0.00	0.00	FRAP
	ATOM	1557	HE22	GLN	2063	-23.899	30.917	6.484	0.00	0.00	FRAP
	ATOM	1558	C	GLN	2063	-24.930	24.278	7.701	1.00	19.53	FRAP

	ATOM	1559	O	GLN	2063	-25.781	23.568	7.181	1.00	22.10	FRAP
	ATOM	1560	N	THR	2064	-23.685	23.880	7.897	1.00	16.77	FRAP
	ATOM	1561	H	THR	2064	-23.114	24.477	8.406	0.00	0.00	FRAP
	ATOM	1562	CA	THR	2064	-23.220	22.593	7.423	1.00	17.61	FRAP
5	ATOM	1563	CB	THR	2064	-21.689	22.551	7.414	1.00	18.02	FRAP
	ATOM	1564	OG1	THR	2064	-21.213	22.465	8.763	1.00	16.37	FRAP
	ATOM	1565	HG1	THR	2064	-21.145	21.529	8.956	0.00	0.00	FRAP
	ATOM	1566	CG2	THR	2064	-21.128	23.812	6.763	1.00	19.18	FRAP
	ATOM	1567	C	THR	2064	-23.743	21.471	8.322	1.00	17.50	FRAP
10	ATOM	1568	O	THR	2064	-24.272	21.725	9.402	1.00	19.82	FRAP
	ATOM	1569	N	LEU	2065	-23.481	20.231	7.922	1.00	17.20	FRAP
	ATOM	1570	H	LEU	2065	-23.146	20.079	7.018	0.00	0.00	FRAP
	ATOM	1571	CA	LEU	2065	-23.813	19.063	8.731	1.00	13.79	FRAP
	ATOM	1572	CB	LEU	2065	-23.667	17.808	7.879	1.00	17.73	FRAP
15	ATOM	1573	CG	LEU	2065	-24.909	16.954	7.614	1.00	18.83	FRAP
	ATOM	1574	CD1	LEU	2065	-26.158	17.819	7.466	1.00	19.10	FRAP
	ATOM	1575	CD2	LEU	2065	-24.658	16.129	6.365	1.00	14.71	FRAP
	ATOM	1576	C	LEU	2065	-22.940	18.949	9.988	1.00	13.22	FRAP
	ATOM	1577	O	LEU	2065	-23.445	18.670	11.070	1.00	12.57	FRAP
20	ATOM	1578	N	LYS	2066	-21.649	19.264	9.848	1.00	9.29	FRAP
	ATOM	1579	H	LYS	2066	-21.297	19.271	8.935	0.00	0.00	FRAP
	ATOM	1580	CA	LYS	2066	-20.707	19.308	10.976	1.00	8.13	FRAP
	ATOM	1581	CB	LYS	2066	-19.297	19.636	10.475	1.00	2.00	FRAP
	ATOM	1582	CG	LYS	2066	-18.442	18.438	10.157	1.00	2.00	FRAP
25	ATOM	1583	CD	LYS	2066	-17.028	18.870	9.846	1.00	2.00	FRAP
	ATOM	1584	CE	LYS	2066	-16.122	17.672	9.553	1.00	9.62	FRAP
	ATOM	1585	NZ	LYS	2066	-16.549	16.861	8.378	1.00	5.28	FRAP
	ATOM	1586	HZ1	LYS	2066	-16.491	17.449	7.520	0.00	0.00	FRAP
	ATOM	1587	HZ2	LYS	2066	-17.527	16.533	8.514	0.00	0.00	FRAP
30	ATOM	1588	HZ3	LYS	2066	-15.912	16.043	8.283	0.00	0.00	FRAP
	ATOM	1589	C	LYS	2066	-21.072	20.317	12.070	1.00	11.53	FRAP
	ATOM	1590	O	LYS	2066	-20.704	20.148	13.226	1.00	16.33	FRAP
	ATOM	1591	N	GLU	2067	-21.548	21.479	11.646	1.00	14.92	FRAP
	ATOM	1592	H	GLU	2067	-21.556	21.672	10.692	0.00	0.00	FRAP
35	ATOM	1593	CA	GLU	2067	-21.998	22.508	12.569	1.00	15.78	FRAP
	ATOM	1594	CB	GLU	2067	-22.143	23.842	11.835	1.00	22.50	FRAP
	ATOM	1595	CG	GLU	2067	-20.877	24.292	11.105	1.00	25.09	FRAP
	ATOM	1596	CD	GLU	2067	-21.032	25.619	10.365	1.00	25.97	FRAP
	ATOM	1597	OE1	GLU	2067	-22.161	26.174	10.309	1.00	16.81	FRAP

ATOM	1598	OE2	GLU	2067	-20.002	26.108	9.844	1.00	26.65	FRAP
ATOM	1599	C	GLU	2067	-23.336	22.108	13.173	1.00	19.42	FRAP
ATOM	1600	O	GLU	2067	-23.693	22.562	14.260	1.00	22.50	FRAP
ATOM	1601	N	THR	2068	-24.096	21.300	12.435	1.00	19.36	FRAP
ATOM	1602	H	THR	2068	-23.847	21.150	11.501	0.00	0.00	FRAP
ATOM	1603	CA	THR	2068	-25.345	20.731	12.940	1.00	18.73	FRAP
ATOM	1604	CB	THR	2068	-26.140	20.025	11.809	1.00	14.88	FRAP
ATOM	1605	OG1	THR	2068	-26.656	21.013	10.912	1.00	16.48	FRAP
ATOM	1606	HG1	THR	2068	-25.961	21.423	10.376	0.00	0.00	FRAP
ATOM	1607	CG2	THR	2068	-27.317	19.239	12.370	1.00	13.69	FRAP
ATOM	1608	C	THR	2068	-25.120	19.751	14.100	1.00	20.11	FRAP
ATOM	1609	O	THR	2068	-25.625	19.971	15.204	1.00	24.18	FRAP
ATOM	1610	N	SER	2069	-24.303	18.724	13.879	1.00	15.42	FRAP
ATOM	1611	H	SER	2069	-23.872	18.626	13.000	0.00	0.00	FRAP
ATOM	1612	CA	SER	2069	-24.066	17.701	14.898	1.00	11.92	FRAP
ATOM	1613	CB	SER	2069	-23.234	16.555	14.315	1.00	3.97	FRAP
ATOM	1614	OG	SER	2069	-21.951	16.993	13.917	1.00	2.00	FRAP
ATOM	1615	HG	SER	2069	-21.427	16.200	13.756	0.00	0.00	FRAP
ATOM	1616	C	SER	2069	-23.404	18.243	16.180	1.00	14.81	FRAP
ATOM	1617	O	SER	2069	-23.865	17.962	17.295	1.00	17.69	FRAP
ATOM	1618	N	PHE	2070	-22.371	19.070	16.018	1.00	12.68	FRAP
ATOM	1619	H	PHE	2070	-21:960	19.083	15.126	0.00	0.00	FRAP
ATOM	1620	CA	PHE	2070	-21.786	19.831	17.132	1.00	6.20	FRAP
ATOM	1621	CB	PHE	2070	-20.732	20.811	16.607	1.00	5.44	FRAP
ATOM	1622	CG	PHE	2070	-20.154	21.726	17.656	1.00	2.00	FRAP
ATOM	1623	CD1	PHE	2070	-18.861	21.521	18.130	1.00	2.00	FRAP
ATOM	1624	CD2	PHE	2070	-20.857	22.848	18.092	1.00	2.00	FRAP
ATOM	1625	CE1	PHE	2070	-18.272	22.419	19.016	1.00	2.00	FRAP
ATOM	1626	CE2	PHE	2070	-20.283	23.748	18.980	1.00	2.00	FRAP
ATOM	1627	CZ	PHE	2070	-18.985	23.534	19.441	1.00	2.00	FRAP
ATOM	1628	C	PHE	2070	-22.856	20.601	17.888	1.00	2.60	FRAP
ATOM	1629	O	PHE	2070	-22.752	20.790	19.082	1.00	7.27	FRAP
ATOM	1630	N	ASN	2071	-23.836	21.135	17.182	1.00	2.01	FRAP
ATOM	1631	H	ASN	2071	-23.831	21.076	16.202	0.00	0.00	FRAP
ATOM	1632	CA	ASN	2071	-24.876	21.880	17.851	1.00	2.00	FRAP
ATOM	1633	CB	ASN	2071	-25.689	22.675	16.841	1.00	7.02	FRAP
ATOM	1634	CG	ASN	2071	-26.604	23.677	17.501	1.00	8.30	FRAP
ATOM	1635	OD1	ASN	2071	-27.805	23.463	17.602	1.00	11.66	FRAP
ATOM	1636	ND2	ASN	2071	-26.035	24.766	17.987	1.00	12.66	FRAP

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ATOM  1637 HD21 ASN 2071     -25.081  24.904  17.878  0.00  0.00      FRAP
ATOM  1638 HD22 ASN 2071     -26.665  25.370  18.419  0.00  0.00      FRAP
ATOM  1639  C   ASN 2071     -25.784  20.959  18.646  1.00  4.16      FRAP
ATOM  1640  O   ASN 2071     -26.258  21.328  19.711  1.00 10.87      FRAP
ATOM  1641  N   GLN 2072     -25.998  19.747  18.143  1.00  8.02      FRAP
ATOM  1642  H   GLN 2072     -25.642  19.564  17.247  0.00  0.00      FRAP
ATOM  1643  CA  GLN 2072     -26.801  18.741  18.845  1.00  8.00      FRAP
ATOM  1644  CB  GLN 2072     -27.061  17.554  17.934  1.00  2.00      FRAP
ATOM  1645  CG  GLN 2072     -28.010  17.884  16.798  1.00  6.79      FRAP
ATOM  1646  CD  GLN 2072     -27.941  16.881  15.665  1.00  8.96      FRAP
ATOM  1647  OE1 GLN 2072     -27.006  16.088  15.570  1.00  4.92      FRAP
ATOM  1648  NE2 GLN 2072     -28.940  16.908  14.798  1.00  6.99      FRAP
ATOM  1649 HE21 GLN 2072     -29.659  17.557  14.919  0.00  0.00      FRAP
ATOM  1650 HE22 GLN 2072     -28.875  16.258  14.072  0.00  0.00      FRAP
ATOM  1651  C   GLN 2072     -26.101  18.262  20.103  1.00 12.51      FRAP
ATOM  1652  O   GLN 2072     -26.693  18.224  21.178  1.00 19.60      FRAP
ATOM  1653  N   ALA 2073     -24.795  18.054  19.978  1.00 14.16      FRAP
ATOM  1654  H   ALA 2073     -24.426  18.142  19.081  0.00  0.00      FRAP
ATOM  1655  CA  ALA 2073     -23.940  17.625  21.077  1.00 14.24      FRAP
ATOM  1656  CB  ALA 2073     -22.583  17.223  20.518  1.00 15.34      FRAP
ATOM  1657  C   ALA 2073     -23.756  18.666  22.196  1.00 15.13      FRAP
ATOM  1658  O   ALA 2073     -24.013  18.383  23.369  1.00 18.26      FRAP
ATOM  1659  N   TYR 2074     -23.228  19.834  21.832  1.00 12.69      FRAP
ATOM  1660  H   TYR 2074     -23.091  19.988  20.874  0.00  0.00      FRAP
ATOM  1661  CA  TYR 2074     -22.791  20.842  22.796  1.00  8.11      FRAP
ATOM  1662  CB  TYR 2074     -21.330  21.206  22.547  1.00  3.13      FRAP
ATOM  1663  CG  TYR 2074     -20.444  20.034  22.216  1.00  8.31      FRAP
ATOM  1664  CD1 TYR 2074     -19.990  19.839  20.918  1.00 10.92      FRAP
ATOM  1665  CE1 TYR 2074     -19.160  18.772  20.591  1.00 12.41      FRAP
ATOM  1666  CD2 TYR 2074     -20.045  19.124  23.197  1.00 11.16      FRAP
ATOM  1667  CE2 TYR 2074     -19.205  18.050  22.882  1.00 12.75      FRAP
ATOM  1668  CZ  TYR 2074     -18.771  17.886  21.569  1.00 12.54      FRAP
ATOM  1669  OH  TYR 2074     -17.960  16.836  21.215  1.00 21.64      FRAP
ATOM  1670  HH  TYR 2074     -17.868  16.773  20.266  0.00  0.00      FRAP
ATOM  1671  C   TYR 2074     -23.618  22.128  22.804  1.00  8.66      FRAP
ATOM  1672  O   TYR 2074     -23.291  23.074  23.509  1.00  9.77      FRAP
ATOM  1673  N   GLY 2075     -24.714  22.153  22.063  1.00 10.37      FRAP
ATOM  1674  H   GLY 2075     -24.997  21.355  21.565  0.00  0.00      FRAP
ATOM  1675  CA  GLY 2075     -25.478  23.380  21.946  1.00 12.34      FRAP
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	ATOM	1676	C	GLY	2075	-26.130	23.796	23.246	1.00	17.07	FRAP
	ATOM	1677	O	GLY	2075	-26.010	24.946	23.660	1.00	24.52	FRAP
	ATOM	1678	N	ARG	2076	-26.770	22.843	23.921	1.00	19.49	FRAP
	ATOM	1679	H	ARG	2076	-26.782	21.950	23.516	0.00	0.00	FRAP
5	ATOM	1680	CA	ARG	2076	-27.476	23.089	25.187	1.00	16.21	FRAP
	ATOM	1681	CB	ARG	2076	-28.162	21.794	25.651	1.00	17.61	FRAP
	ATOM	1682	CG	ARG	2076	-28.703	21.826	27.072	1.00	25.98	FRAP
	ATOM	1683	CD	ARG	2076	-29.913	20.929	27.228	1.00	33.40	FRAP
	ATOM	1684	NE	ARG	2076	-31.135	21.578	26.754	1.00	44.19	FRAP
10	ATOM	1685	HE	ARG	2076	-31.060	22.233	26.029	0.00	0.00	FRAP
	ATOM	1686	CZ	ARG	2076	-32.351	21.341	27.241	1.00	50.69	FRAP
	ATOM	1687	NH1	ARG	2076	-33.396	22.014	26.769	1.00	53.46	FRAP
	ATOM	1688	HH11	ARG	2076	-33.274	22.698	26.051	0.00	0.00	FRAP
	ATOM	1689	HH12	ARG	2076	-34.308	21.839	27.144	0.00	0.00	FRAP
15	ATOM	1690	NH2	ARG	2076	-32.532	20.415	28.180	1.00	51.70	FRAP
	ATOM	1691	HH21	ARG	2076	-31.750	19.895	28.525	0.00	0.00	FRAP
	ATOM	1692	HH22	ARG	2076	-33.446	20.249	28.551	0.00	0.00	FRAP
	ATOM	1693	C	ARG	2076	-26.574	23.640	26.305	1.00	11.79	FRAP
	ATOM	1694	O	ARG	2076	-26.861	24.680	26.885	1.00	11.52	FRAP
20	ATOM	1695	N	ASP	2077	-25.490	22.936	26.604	1.00	8.15	FRAP
	ATOM	1696	H	ASP	2077	-25.346	22.086	26.144	0.00	0.00	FRAP
	ATOM	1697	CA	ASP	2077	-24.526	23.394	27.594	1.00	6.48	FRAP
	ATOM	1698	CB	ASP	2077	-23.332	22.448	27.637	1.00	5.61	FRAP
	ATOM	1699	CG	ASP	2077	-23.615	21.196	28.425	1.00	10.00	FRAP
25	ATOM	1700	OD1	ASP	2077	-24.726	21.096	28.999	1.00	9.97	FRAP
	ATOM	1701	OD2	ASP	2077	-22.724	20.317	28.479	1.00	12.06	FRAP
	ATOM	1702	C	ASP	2077	-24.035	24.809	27.331	1.00	8.55	FRAP
	ATOM	1703	O	ASP	2077	-24.126	25.669	28.201	1.00	13.05	FRAP
	ATOM	1704	N	LEU	2078	-23.544	25.058	26.123	1.00	6.49	FRAP
30	ATOM	1705	H	LEU	2078	-23.477	24.330	25.469	0.00	0.00	FRAP
	ATOM	1706	CA	LEU	2078	-23.064	26.386	25.752	1.00	4.74	FRAP
	ATOM	1707	CB	LEU	2078	-22.495	26.364	24.333	1.00	3.18	FRAP
	ATOM	1708	CG	LEU	2078	-21.161	25.653	24.084	1.00	2.91	FRAP
	ATOM	1709	CD1	LEU	2078	-20.928	25.574	22.593	1.00	2.37	FRAP
35	ATOM	1710	CD2	LEU	2078	-20.010	26.387	24.764	1.00	2.00	FRAP
	ATOM	1711	C	LEU	2078	-24.146	27.466	25.862	1.00	4.72	FRAP
	ATOM	1712	O	LEU	2078	-23.847	28.626	26.118	1.00	2.64	FRAP
	ATOM	1713	N	MET	2079	-25.401	27.091	25.651	1.00	7.76	FRAP
	ATOM	1714	H	MET	2079	-25.579	26.181	25.326	0.00	0.00	FRAP

	ATOM	1715	CA	MET	2079	-26.507	28.022	25.850	1.00	14.65	FRAP
	ATOM	1716	CB	MET	2079	-27.803	27.434	25.295	1.00	18.67	FRAP
	ATOM	1717	CG	MET	2079	-28.999	28.367	25.363	1.00	25.96	FRAP
	ATOM	1718	SD	MET	2079	-29.718	28.677	23.724	1.00	40.57	FRAP
5	ATOM	1719	CE	MET	2079	-30.358	27.004	23.294	1.00	36.64	FRAP
	ATOM	1720	C	MET	2079	-26.686	28.344	27.330	1.00	17.59	FRAP
	ATOM	1721	O	MET	2079	-26.714	29.505	27.716	1.00	21.68	FRAP
	ATOM	1722	N	GLU	2080	-26.769	27.308	28.158	1.00	18.54	FRAP
	ATOM	1723	H	GLU	2080	-26.733	26.408	27.770	0.00	0.00	FRAP
10	ATOM	1724	CA	GLU	2080	-26.928	27.477	29.599	1.00	18.17	FRAP
	ATOM	1725	CB	GLU	2080	-27.006	26.111	30.286	1.00	24.46	FRAP
	ATOM	1726	CG	GLU	2080	-27.581	26.144	31.708	1.00	33.04	FRAP
	ATOM	1727	CD	GLU	2080	-27.199	24.914	32.530	1.00	37.28	FRAP
	ATOM	1728	OE1	GLU	2080	-26.827	25.080	33.714	1.00	39.48	FRAP
15	ATOM	1729	OE2	GLU	2080	-27.253	23.783	31.991	1.00	40.40	FRAP
	ATOM	1730	C	GLU	2080	-25.773	28.284	30.191	1.00	16.44	FRAP
	ATOM	1731	O	GLU	2080	-25.995	29.230	30.940	1.00	17.68	FRAP
	ATOM	1732	N	ALA	2081	-24.555	27.981	29.756	1.00	15.30	FRAP
	ATOM	1733	H	ALA	2081	-24.449	27.180	29.211	0.00	0.00	FRAP
20	ATOM	1734	CA	ALA	2081	-23.375	28.743	30.149	1.00	12.75	FRAP
	ATOM	1735	CB	ALA	2081	-22.163	28.263	29.373	1.00	8.47	FRAP
	ATOM	1736	C	ALA	2081	-23.591	30.233	29.912	1.00	14.17	FRAP
	ATOM	1737	O	ALA	2081	-23.284	31.057	30.767	1.00	17.02	FRAP
	ATOM	1738	N	GLN	2082	-24.253	30.560	28.809	1.00	16.91	FRAP
25	ATOM	1739	H	GLN	2082	-24.566	29.833	28.233	0.00	0.00	FRAP
	ATOM	1740	CA	GLN	2082	-24.557	31.948	28.477	1.00	18.00	FRAP
	ATOM	1741	CB	GLN	2082	-25.085	32.032	27.048	1.00	22.74	FRAP
	ATOM	1742	CG	GLN	2082	-25.879	33.280	26.739	1.00	26.79	FRAP
	ATOM	1743	CD	GLN	2082	-26.176	33.408	25.268	1.00	31.68	FRAP
30	ATOM	1744	OE1	GLN	2082	-25.360	33.930	24.509	1.00	29.64	FRAP
	ATOM	1745	NE2	GLN	2082	-27.299	32.846	24.838	1.00	31.52	FRAP
	ATOM	1746	HE21	GLN	2082	-27.890	32.386	25.460	0.00	0.00	FRAP
	ATOM	1747	HE22	GLN	2082	-27.467	32.967	23.886	0.00	0.00	FRAP
	ATOM	1748	C	GLN	2082	-25.558	32.584	29.439	1.00	17.54	FRAP
35	ATOM	1749	O	GLN	2082	-25.442	33.759	29.768	1.00	19.50	FRAP
	ATOM	1750	N	GLU	2083	-26.551	31.819	29.875	1.00	18.34	FRAP
	ATOM	1751	H	GLU	2083	-26.603	30.892	29.552	0.00	0.00	FRAP
	ATOM	1752	CA	GLU	2083	-27.523	32.342	30.826	1.00	19.36	FRAP
	ATOM	1753	CB	GLU	2083	-28.680	31.362	31.021	1.00	26.08	FRAP

	ATOM	1754	CG	GLU	2083	-29.802	31.897	31.915	1.00	40.13	FRAP
	ATOM	1755	CD	GLU	2083	-30.388	33.226	31.428	1.00	46.90	FRAP
	ATOM	1756	OE1	GLU	2083	-30.392	34.207	32.209	1.00	48.07	FRAP
	ATOM	1757	OE2	GLU	2083	-30.878	33.280	30.279	1.00	52.86	FRAP
	ATOM	1758	C	GLU	2083	-26.863	32.651	32.166	1.00	13.37	FRAP
	ATOM	1759	O	GLU	2083	-27.102	33.701	32.747	1.00	17.15	FRAP
	ATOM	1760	N	TRP	2084	-25.915	31.817	32.563	1.00	6.62	FRAP
	ATOM	1761	H	TRP	2084	-25.769	30.992	32.047	0.00	0.00	FRAP
	ATOM	1762	CA	TRP	2084	-25.139	32.069	33.761	1.00	3.33	FRAP
	ATOM	1763	CB	TRP	2084	-24.190	30.914	34.037	1.00	5.07	FRAP
	ATOM	1764	CG	TRP	2084	-24.879	29.734	34.575	1.00	6.00	FRAP
	ATOM	1765	CD2	TRP	2084	-25.606	29.664	35.801	1.00	10.76	FRAP
	ATOM	1766	CE2	TRP	2084	-26.292	28.433	35.807	1.00	14.65	FRAP
	ATOM	1767	CE3	TRP	2084	-25.765	30.533	36.887	1.00	9.81	FRAP
	ATOM	1768	CD1	TRP	2084	-25.110	28.564	33.924	1.00	10.88	FRAP
	ATOM	1769	NE1	TRP	2084	-25.972	27.781	34.646	1.00	17.13	FRAP
	ATOM	1770	HE1	TRP	2084	-26.397	26.972	34.309	0.00	0.00	FRAP
	ATOM	1771	CZ2	TRP	2084	-27.129	28.050	36.853	1.00	14.61	FRAP
	ATOM	1772	CZ3	TRP	2084	-26.597	30.156	37.923	1.00	11.54	FRAP
	ATOM	1773	CH2	TRP	2084	-27.272	28.924	37.899	1.00	16.36	FRAP
	ATOM	1774	C	TRP	2084	-24.348	33.355	33.677	1.00	4.82	FRAP
	ATOM	1775	O	TRP	2084	-24.240	34.076	34.665	1.00	10.80	FRAP
	ATOM	1776	N	CYS	2085	-23.760	33.625	32.514	1.00	7.15	FRAP
	ATOM	1777	H	CYS	2085	-23.725	32.895	31.856	0.00	0.00	FRAP
	ATOM	1778	CA	CYS	2085	-23.062	34.894	32.274	1.00	7.94	FRAP
	ATOM	1779	CB	CYS	2085	-22.329	34.868	30.935	1.00	2.21	FRAP
	ATOM	1780	SG	CYS	2085	-20.748	34.024	30.993	1.00	14.42	FRAP
	ATOM	1781	C	CYS	2085	-24.030	36.070	32.284	1.00	11.28	FRAP
	ATOM	1782	O	CYS	2085	-23.718	37.138	32.813	1.00	13.68	FRAP
	ATOM	1783	N	ARG	2086	-25.214	35.864	31.718	1.00	10.58	FRAP
	ATOM	1784	H	ARG	2086	-25.382	35.014	31.259	0.00	0.00	FRAP
	ATOM	1785	CA	ARG	2086	-26.250	36.878	31.749	1.00	11.82	FRAP
	ATOM	1786	CB	ARG	2086	-27.476	36.405	30.970	1.00	16.71	FRAP
	ATOM	1787	CG	ARG	2086	-27.279	36.429	29.458	1.00	22.27	FRAP
	ATOM	1788	CD	ARG	2086	-28.160	35.398	28.768	1.00	36.61	FRAP
	ATOM	1789	NE	ARG	2086	-29.300	35.986	28.060	1.00	45.02	FRAP
	ATOM	1790	HE	ARG	2086	-29.553	36.906	28.280	0.00	0.00	FRAP
	ATOM	1791	CZ	ARG	2086	-30.003	35.357	27.118	1.00	49.39	FRAP
	ATOM	1792	NH1	ARG	2086	-31.021	35.971	26.523	1.00	48.26	FRAP

ATOM	1793	HH11	ARG	2086	-31.246	36.916	26.762	0.00	0.00	FRAP
ATOM	1794	HH12	ARG	2086	-31.538	35.499	25.809	0.00	0.00	FRAP
ATOM	1795	NH2	ARG	2086	-29.673	34.120	26.747	1.00	49.75	FRAP
ATOM	1796	HH21	ARG	2086	-28.913	33.645	27.190	0.00	0.00	FRAP
ATOM	1797	HH22	ARG	2086	-30.218	33.649	26.053	0.00	0.00	FRAP
ATOM	1798	C	ARG	2086	-26.618	37.180	33.193	1.00	11.93	FRAP
ATOM	1799	O	ARG	2086	-26.536	38.325	33.629	1.00	14.05	FRAP
ATOM	1800	N	LYS	2087	-26.792	36.120	33.976	1.00	14.39	FRAP
ATOM	1801	H	LYS	2087	-26.697	35.240	33.583	0.00	0.00	FRAP
ATOM	1802	CA	LYS	2087	-27.104	36.240	35.401	1.00	11.99	FRAP
ATOM	1803	CB	LYS	2087	-27.217	34.858	36.040	1.00	12.74	FRAP
ATOM	1804	CG	LYS	2087	-28.510	34.139	35.778	1.00	13.98	FRAP
ATOM	1805	CD	LYS	2087	-28.412	32.700	36.270	1.00	17.19	FRAP
ATOM	1806	CE	LYS	2087	-29.760	31.998	36.220	1.00	26.67	FRAP
ATOM	1807	NZ	LYS	2087	-29.640	30.517	36.341	1.00	33.46	FRAP
ATOM	1808	HZ1	LYS	2087	-29.184	30.284	37.245	0.00	0.00	FRAP
ATOM	1809	HZ2	LYS	2087	-29.051	30.158	35.561	0.00	0.00	FRAP
ATOM	1810	HZ3	LYS	2087	-30.581	30.076	36.301	0.00	0.00	FRAP
ATOM	1811	C	LYS	2087	-26.038	37.041	36.144	1.00	9.73	FRAP
ATOM	1812	O	LYS	2087	-26.356	37.859	37.000	1.00	12.76	FRAP
ATOM	1813	N	TYR	2088	-24.771	36.803	35.821	1.00	7.02	FRAP
ATOM	1814	H	TYR	2088	-24.578	36.057	35.209	0.00	0.00	FRAP
ATOM	1815	CA	TYR	2088	-23.693	37.592	36.407	1.00	12.48	FRAP
ATOM	1816	CB	TYR	2088	-22.327	37.135	35.892	1.00	9.00	FRAP
ATOM	1817	CG	TYR	2088	-21.194	38.013	36.386	1.00	11.53	FRAP
ATOM	1818	CD1	TYR	2088	-20.780	37.953	37.712	1.00	13.53	FRAP
ATOM	1819	CE1	TYR	2088	-19.817	38.822	38.205	1.00	13.24	FRAP
ATOM	1820	CD2	TYR	2088	-20.603	38.967	35.553	1.00	9.73	FRAP
ATOM	1821	CE2	TYR	2088	-19.631	39.835	36.032	1.00	8.20	FRAP
ATOM	1822	CZ	TYR	2088	-19.248	39.758	37.364	1.00	14.19	FRAP
ATOM	1823	OH	TYR	2088	-18.308	40.621	37.881	1.00	21.06	FRAP
ATOM	1824	HH	TYR	2088	-17.982	41.148	37.148	0.00	0.00	FRAP
ATOM	1825	C	TYR	2088	-23.872	39.079	36.109	1.00	15.40	FRAP
ATOM	1826	O	TYR	2088	-23.750	39.921	37.000	1.00	21.76	FRAP
ATOM	1827	N	MET	2089	-24.238	39.383	34.870	1.00	14.77	FRAP
ATOM	1828	H	MET	2089	-24.371	38.652	34.223	0.00	0.00	FRAP
ATOM	1829	CA	MET	2089	-24.442	40.757	34.446	1.00	13.39	FRAP
ATOM	1830	CB	MET	2089	-24.813	40.789	32.962	1.00	11.91	FRAP
ATOM	1831	CG	MET	2089	-23.637	40.488	32.049	1.00	11.63	FRAP

	ATOM	1832	SD	MET	2089	-24.124	40.080	30.365	1.00	13.84	FRAP
	ATOM	1833	CE	MET	2089	-22.620	39.331	29.759	1.00	2.00	FRAP
	ATOM	1834	C	MET	2089	-25.500	41.475	35.272	1.00	11.34	FRAP
	ATOM	1835	O	MET	2089	-25.392	42.669	35.511	1.00	16.85	FRAP
	ATOM	1836	N	LYS	2090	-26.475	40.728	35.775	1.00	13.58	FRAP
	ATOM	1837	H	LYS	2090	-26.475	39.771	35.559	0.00	0.00	FRAP
	ATOM	1838	CA	LYS	2090	-27.591	41.322	36.506	1.00	17.01	FRAP
	ATOM	1839	CB	LYS	2090	-28.886	40.552	36.209	1.00	17.48	FRAP
	ATOM	1840	CG	LYS	2090	-29.218	39.436	37.207	1.00	30.54	FRAP
	ATOM	1841	CD	LYS	2090	-30.240	39.892	38.254	1.00	39.03	FRAP
	ATOM	1842	CE	LYS	2090	-30.140	39.078	39.545	1.00	40.52	FRAP
	ATOM	1843	NZ	LYS	2090	-30.477	39.893	40.756	1.00	38.43	FRAP
	ATOM	1844	HZ1	LYS	2090	-31.451	40.248	40.672	0.00	0.00	FRAP
	ATOM	1845	HZ2	LYS	2090	-29.826	40.700	40.829	0.00	0.00	FRAP
	ATOM	1846	HZ3	LYS	2090	-30.396	39.308	41.612	0.00	0.00	FRAP
	ATOM	1847	C	LYS	2090	-27.371	41.420	38.023	1.00	18.18	FRAP
	ATOM	1848	O	LYS	2090	-28.022	42.230	38.695	1.00	16.27	FRAP
	ATOM	1849	N	SER	2091	-26.466	40.597	38.554	1.00	18.19	FRAP
	ATOM	1850	H	SER	2091	-25.955	40.047	37.923	0.00	0.00	FRAP
	ATOM	1851	CA	SER	2091	-26.302	40.464	40.008	1.00	16.08	FRAP
	ATOM	1852	CB	SER	2091	-26.662	39.051	40.465	1.00	15.61	FRAP
	ATOM	1853	OG	SER	2091	-25.722	38.108	39.982	1.00	18.00	FRAP
	ATOM	1854	HG	SER	2091	-26.010	37.832	39.096	0.00	0.00	FRAP
	ATOM	1855	C	SER	2091	-24.917	40.794	40.537	1.00	14.61	FRAP
	ATOM	1856	O	SER	2091	-24.761	41.071	41.724	1.00	16.95	FRAP
	ATOM	1857	N	GLY	2092	-23.903	40.637	39.691	1.00	10.93	FRAP
	ATOM	1858	H	GLY	2092	-24.107	40.356	38.784	0.00	0.00	FRAP
	ATOM	1859	CA	GLY	2092	-22.536	40.883	40.117	1.00	12.47	FRAP
	ATOM	1860	C	GLY	2092	-22.009	39.837	41.083	1.00	13.42	FRAP
	ATOM	1861	O	GLY	2092	-20.913	39.974	41.622	1.00	11.96	FRAP
	ATOM	1862	N	ASN	2093	-22.701	38.704	41.127	1.00	14.42	FRAP
	ATOM	1863	H	ASN	2093	-23.481	38.626	40.514	0.00	0.00	FRAP
	ATOM	1864	CA	ASN	2093	-22.465	37.664	42.114	1.00	15.72	FRAP
	ATOM	1865	CB	ASN	2093	-23.572	36.626	42.021	1.00	15.84	FRAP
	ATOM	1866	CG	ASN	2093	-23.884	35.977	43.353	1.00	16.87	FRAP
	ATOM	1867	OD1	ASN	2093	-25.031	35.976	43.798	1.00	23.23	FRAP
	ATOM	1868	ND2	ASN	2093	-22.879	35.381	43.975	1.00	9.23	FRAP
	ATOM	1869	HD21	ASN	2093	-21.955	35.362	43.700	0.00	0.00	FRAP
	ATOM	1870	HD22	ASN	2093	-23.187	35.027	44.822	0.00	0.00	FRAP

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ATOM   1871  C   ASN 2093     -21.112  36.959  42.015  1.00 20.92      FRAP
ATOM   1872  O   ASN 2093     -20.599  36.466  43.015  1.00 28.74      FRAP
ATOM   1873  N   VAL 2094     -20.653  36.711  40.797  1.00 18.46      FRAP
ATOM   1874  H   VAL 2094     -21.105  37.113  40.045  0.00  0.00      FRAP
ATOM   1875  CA  VAL 2094     -19.386  36.003  40.528  1.00 19.15      FRAP
ATOM   1876  CB  VAL 2094     -18.134  36.636  41.223  1.00 17.65      FRAP
ATOM   1877  CG1 VAL 2094     -17.885  36.035  42.612  1.00 19.24      FRAP
ATOM   1878  CG2 VAL 2094     -16.911  36.422  40.333  1.00 22.37      FRAP
ATOM   1879  C   VAL 2094     -19.390  34.508  40.807  1.00 17.55      FRAP
ATOM   1880  O   VAL 2094     -18.534  33.779  40.311  1.00 20.43      FRAP
ATOM   1881  N   LYS 2095     -20.415  34.016  41.485  1.00 16.99      FRAP
ATOM   1882  H   LYS 2095     -20.859  34.593  42.164  0.00  0.00      FRAP
ATOM   1883  CA  LYS 2095     -20.615  32.570  41.511  1.00 19.09      FRAP
ATOM   1884  CB  LYS 2095     -21.166  32.125  42.869  1.00 24.46      FRAP
ATOM   1885  CG  LYS 2095     -20.193  31.221  43.633  1.00 33.72      FRAP
ATOM   1886  CD  LYS 2095     -18.736  31.682  43.507  1.00 32.25      FRAP
ATOM   1887  CE  LYS 2095     -17.771  30.625  44.033  1.00 37.61      FRAP
ATOM   1888  NZ  LYS 2095     -17.512  29.527  43.054  1.00 34.92      FRAP
ATOM   1889  HZ1 LYS 2095     -17.131  29.930  42.177  0.00  0.00      FRAP
ATOM   1890  HZ2 LYS 2095     -18.395  29.025  42.842  0.00  0.00      FRAP
ATOM   1891  HZ3 LYS 2095     -16.816  28.873  43.458  0.00  0.00      FRAP
ATOM   1892  C   LYS 2095     -21.515  32.087  40.378  1.00 16.91      FRAP
ATOM   1893  O   LYS 2095     -21.621  30.893  40.110  1.00 15.63      FRAP
ATOM   1894  N   ASP 2096     -22.168  33.029  39.710  1.00 14.55      FRAP
ATOM   1895  H   ASP 2096     -22.269  33.893  40.141  0.00  0.00      FRAP
ATOM   1896  CA  ASP 2096     -22.850  32.737  38.459  1.00 11.12      FRAP
ATOM   1897  CB  ASP 2096     -23.799  33.868  38.099  1.00 12.16      FRAP
ATOM   1898  CG  ASP 2096     -24.973  33.956  39.042  1.00 14.76      FRAP
ATOM   1899  OD1 ASP 2096     -25.630  32.925  39.259  1.00 18.49      FRAP
ATOM   1900  OD2 ASP 2096     -25.238  35.055  39.567  1.00 24.14      FRAP
ATOM   1901  C   ASP 2096     -21.837  32.538  37.339  1.00 10.59      FRAP
ATOM   1902  O   ASP 2096     -21.903  31.563  36.590  1.00 13.81      FRAP
ATOM   1903  N   LEU 2097     -20.816  33.386  37.326  1.00  7.24      FRAP
ATOM   1904  H   LEU 2097     -20.814  34.129  37.956  0.00  0.00      FRAP
ATOM   1905  CA  LEU 2097     -19.723  33.244  36.383  1.00  7.03      FRAP
ATOM   1906  CB  LEU 2097     -18.701  34.357  36.591  1.00  2.85      FRAP
ATOM   1907  CG  LEU 2097     -18.252  35.073  35.317  1.00  7.43      FRAP
ATOM   1908  CD1 LEU 2097     -19.451  35.345  34.428  1.00  2.68      FRAP
ATOM   1909  CD2 LEU 2097     -17.543  36.371  35.661  1.00  6.68      FRAP
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ATOM	1910	C	LEU	2097	-19.056	31.873	36.504	1.00	12.75	FRAP
ATOM	1911	O	LEU	2097	-18.854	31.190	35.499	1.00	17.71	FRAP
ATOM	1912	N	THR	2098	-18.847	31.410	37.735	1.00	13.89	FRAP
ATOM	1913	H	THR	2098	-19.017	31.985	38.512	0.00	0.00	FRAP
ATOM	1914	CA	THR	2098	-18.266	30.082	37.954	1.00	14.50	FRAP
ATOM	1915	CB	THR	2098	-17.866	29.853	39.429	1.00	18.86	FRAP
ATOM	1916	OG1	THR	2098	-18.952	30.231	40.288	1.00	27.76	FRAP
ATOM	1917	HG1	THR	2098	-19.663	29.576	40.325	0.00	0.00	FRAP
ATOM	1918	CG2	THR	2098	-16.624	30.666	39.781	1.00	14.88	FRAP
ATOM	1919	C	THR	2098	-19.187	28.940	37.521	1.00	14.65	FRAP
ATOM	1920	O	THR	2098	-18.733	27.967	36.924	1.00	20.42	FRAP
ATOM	1921	N	GLN	2099	-20.486	29.070	37.772	1.00	13.41	FRAP
ATOM	1922	H	GLN	2099	-20.807	29.834	38.297	0.00	0.00	FRAP
ATOM	1923	CA	GLN	2099	-21.443	28.076	37.293	1.00	10.97	FRAP
ATOM	1924	CB	GLN	2099	-22.843	28.371	37.838	1.00	19.13	FRAP
ATOM	1925	CG	GLN	2099	-23.423	27.264	38.720	1.00	26.63	FRAP
ATOM	1926	CD	GLN	2099	-23.315	25.887	38.084	1.00	33.37	FRAP
ATOM	1927	OE1	GLN	2099	-22.604	25.017	38.580	1.00	35.83	FRAP
ATOM	1928	NE2	GLN	2099	-23.989	25.697	36.959	1.00	38.47	FRAP
ATOM	1929	HE21	GLN	2099	-24.521	26.407	36.558	0.00	0.00	FRAP
ATOM	1930	HE22	GLN	2099	-23.848	24.808	36.587	0.00	0.00	FRAP
ATOM	1931	C	GLN	2099	-21.478	28.072	35.768	1.00	9.33	FRAP
ATOM	1932	O	GLN	2099	-21.842	27.085	35.147	1.00	13.05	FRAP
ATOM	1933	N	ALA	2100	-21.146	29.211	35.178	1.00	9.52	FRAP
ATOM	1934	H	ALA	2100	-21.074	30.018	35.723	0.00	0.00	FRAP
ATOM	1935	CA	ALA	2100	-21.016	29.323	33.738	1.00	3.77	FRAP
ATOM	1936	CB	ALA	2100	-20.953	30.796	33.348	1.00	2.00	FRAP
ATOM	1937	C	ALA	2100	-19.760	28.586	33.277	1.00	2.86	FRAP
ATOM	1938	O	ALA	2100	-19.823	27.736	32.394	1.00	2.63	FRAP
ATOM	1939	N	TRP	2101	-18.659	28.801	33.988	1.00	2.00	FRAP
ATOM	1940	H	TRP	2101	-18.717	29.421	34.743	0.00	0.00	FRAP
ATOM	1941	CA	TRP	2101	-17.367	28.222	33.627	1.00	3.21	FRAP
ATOM	1942	CB	TRP	2101	-16.263	29.010	34.300	1.00	3.18	FRAP
ATOM	1943	CG	TRP	2101	-15.704	30.029	33.420	1.00	4.37	FRAP
ATOM	1944	CD2	TRP	2101	-15.003	29.798	32.198	1.00	5.80	FRAP
ATOM	1945	CE2	TRP	2101	-14.676	31.057	31.662	1.00	7.80	FRAP
ATOM	1946	CE3	TRP	2101	-14.625	28.646	31.500	1.00	5.41	FRAP
ATOM	1947	CD1	TRP	2101	-15.775	31.378	33.581	1.00	5.99	FRAP
ATOM	1948	NE1	TRP	2101	-15.158	32.008	32.525	1.00	13.05	FRAP

	ATOM	1949	HE1	TRP	2101	-15.113	32.979	32.395	0.00	0.00	FRAP
	ATOM	1950	CZ2	TRP	2101	-13.993	31.197	30.456	1.00	6.76	FRAP
	ATOM	1951	CZ3	TRP	2101	-13.951	28.786	30.301	1.00	3.13	FRAP
	ATOM	1952	CH2	TRP	2101	-13.644	30.052	29.791	1.00	6.31	FRAP
5	ATOM	1953	C	TRP	2101	-17.206	26.736	33.960	1.00	8.69	FRAP
	ATOM	1954	O	TRP	2101	-16.274	26.065	33.501	1.00	10.67	FRAP
	ATOM	1955	N	ASP	2102	-18.091	26.240	34.807	1.00	8.35	FRAP
	ATOM	1956	H	ASP	2102	-18.571	26.864	35.388	0.00	0.00	FRAP
	ATOM	1957	CA	ASP	2102	-18.235	24.815	35.005	1.00	9.05	FRAP
10	ATOM	1958	CB	ASP	2102	-19.277	24.564	36.099	1.00	13.12	FRAP
	ATOM	1959	CG	ASP	2102	-19.127	23.207	36.759	1.00	16.43	FRAP
	ATOM	1960	OD1	ASP	2102	-20.084	22.779	37.436	1.00	23.14	FRAP
	ATOM	1961	OD2	ASP	2102	-18.048	22.585	36.637	1.00	18.55	FRAP
	ATOM	1962	C	ASP	2102	-18.688	24.180	33.686	1.00	10.27	FRAP
15	ATOM	1963	O	ASP	2102	-18.144	23.158	33.248	1.00	11.33	FRAP
	ATOM	1964	N	LEU	2103	-19.646	24.828	33.029	1.00	8.01	FRAP
	ATOM	1965	H	LEU	2103	-19.988	25.662	33.421	0.00	0.00	FRAP
	ATOM	1966	CA	LEU	2103	-20.230	24.302	31.794	1.00	7.80	FRAP
	ATOM	1967	CB	LEU	2103	-21.589	24.951	31.537	1.00	2.00	FRAP
20	ATOM	1968	CG	LEU	2103	-22.694	24.551	32.512	1.00	2.00	FRAP
	ATOM	1969	CD1	LEU	2103	-23.659	25.697	32.675	1.00	2.04	FRAP
	ATOM	1970	CD2	LEU	2103	-23.417	23.318	32.012	1.00	2.00	FRAP
	ATOM	1971	C	LEU	2103	-19.314	24.486	30.577	1.00	7.45	FRAP
	ATOM	1972	O	LEU	2103	-19.177	23.580	29.756	1.00	5.72	FRAP
25	ATOM	1973	N	TYR	2104	-18.594	25.602	30.530	1.00	6.39	FRAP
	ATOM	1974	H	TYR	2104	-18.814	26.319	31.162	0.00	0.00	FRAP
	ATOM	1975	CA	TYR	2104	-17.605	25.821	29.482	1.00	7.03	FRAP
	ATOM	1976	CB	TYR	2104	-16.987	27.215	29.602	1.00	7.14	FRAP
	ATOM	1977	CG	TYR	2104	-17.865	28.342	29.108	1.00	4.21	FRAP
30	ATOM	1978	CD1	TYR	2104	-18.003	29.508	29.852	1.00	7.88	FRAP
	ATOM	1979	CE1	TYR	2104	-18.772	30.564	29.400	1.00	5.53	FRAP
	ATOM	1980	CD2	TYR	2104	-18.535	28.256	27.888	1.00	2.00	FRAP
	ATOM	1981	CE2	TYR	2104	-19.316	29.308	27.423	1.00	3.76	FRAP
	ATOM	1982	CZ	TYR	2104	-19.419	30.462	28.187	1.00	8.86	FRAP
35	ATOM	1983	OH	TYR	2104	-20.122	31.548	27.727	1.00	12.11	FRAP
	ATOM	1984	HH	TYR	2104	-20.693	31.333	27.011	0.00	0.00	FRAP
	ATOM	1985	C	TYR	2104	-16.506	24.771	29.555	1.00	9.25	FRAP
	ATOM	1986	O	TYR	2104	-16.102	24.216	28.536	1.00	12.91	FRAP
	ATOM	1987	N	TYR	2105	-16.054	24.475	30.771	1.00	12.79	FRAP

	ATOM	1988	H	TYR	2105	-16.371	25.002	31.536	0.00	0.00	FRAP
	ATOM	1989	CA	TYR	2105	-15.030	23.452	30.996	1.00	10.70	FRAP
	ATOM	1990	CB	TYR	2105	-14.680	23.376	32.481	1.00	7.06	FRAP
	ATOM	1991	CG	TYR	2105	-13.496	22.488	32.765	1.00	4.50	FRAP
	ATOM	1992	CD1	TYR	2105	-12.288	22.693	32.111	1.00	8.17	FRAP
	ATOM	1993	CE1	TYR	2105	-11.184	21.892	32.360	1.00	12.33	FRAP
	ATOM	1994	CD2	TYR	2105	-13.579	21.446	33.684	1.00	6.11	FRAP
	ATOM	1995	CE2	TYR	2105	-12.472	20.629	33.946	1.00	12.32	FRAP
	ATOM	1996	CZ	TYR	2105	-11.276	20.866	33.279	1.00	15.17	FRAP
	ATOM	1997	OH	TYR	2105	-10.155	20.113	33.542	1.00	21.26	FRAP
	ATOM	1998	HH	TYR	2105	-9.397	20.447	33.059	0.00	0.00	FRAP
	ATOM	1999	C	TYR	2105	-15.479	22.070	30.515	1.00	10.02	FRAP
	ATOM	2000	O	TYR	2105	-14.702	21.307	29.942	1.00	11.77	FRAP
	ATOM	2001	N	HIS	2106	-16.746	21.759	30.737	1.00	9.87	FRAP
	ATOM	2002	H	HIS	2106	-17.288	22.402	31.250	0.00	0.00	FRAP
	ATOM	2003	CA	HIS	2106	-17.298	20.488	30.314	1.00	11.64	FRAP
	ATOM	2004	CB	HIS	2106	-18.705	20.326	30.881	1.00	15.15	FRAP
	ATOM	2005	CG	HIS	2106	-19.294	18.971	30.664	1.00	24.44	FRAP
	ATOM	2006	CD2	HIS	2106	-20.529	18.588	30.259	1.00	25.83	FRAP
	ATOM	2007	ND1	HIS	2106	-18.578	17.808	30.865	1.00	28.70	FRAP
	ATOM	2008	HD1	HIS	2106	-17.628	17.736	31.114	0.00	0.00	FRAP
	ATOM	2009	CE1	HIS	2106	-19.346	16.767	30.595	1.00	28.91	FRAP
	ATOM	2010	NE2	HIS	2106	-20.535	17.214	30.226	1.00	31.03	FRAP
	ATOM	2011	HE2	HIS	2106	-21.295	16.644	29.972	0.00	0.00	FRAP
	ATOM	2012	C	HIS	2106	-17.315	20.332	28.787	1.00	14.72	FRAP
	ATOM	2013	O	HIS	2106	-16.928	19.284	28.273	1.00	17.34	FRAP
	ATOM	2014	N	VAL	2107	-17.768	21.355	28.062	1.00	13.33	FRAP
	ATOM	2015	H	VAL	2107	-18.077	22.171	28.519	0.00	0.00	FRAP
	ATOM	2016	CA	VAL	2107	-17.797	21.281	26.599	1.00	10.31	FRAP
	ATOM	2017	CB	VAL	2107	-18.640	22.425	25.963	1.00	9.70	FRAP
	ATOM	2018	CG1	VAL	2107	-20.082	22.296	26.372	1.00	11.91	FRAP
	ATOM	2019	CG2	VAL	2107	-18.116	23.780	26.371	1.00	15.79	FRAP
	ATOM	2020	C	VAL	2107	-16.384	21.294	26.009	1.00	10.92	FRAP
	ATOM	2021	O	VAL	2107	-16.047	20.456	25.172	1.00	11.27	FRAP
	ATOM	2022	N	PHE	2108	-15.518	22.127	26.576	1.00	9.62	FRAP
	ATOM	2023	H	PHE	2108	-15.849	22.771	27.234	0.00	0.00	FRAP
	ATOM	2024	CA	PHE	2108	-14.109	22.164	26.187	1.00	8.05	FRAP
	ATOM	2025	CB	PHE	2108	-13.371	23.223	27.007	1.00	4.20	FRAP
	ATOM	2026	CG	PHE	2108	-11.923	23.366	26.651	1.00	2.00	FRAP

	ATOM	2027	CD1	PHE	2108	-11.519	24.292	25.702	1.00	4.15	FRAP
	ATOM	2028	CD2	PHE	2108	-10.961	22.606	27.295	1.00	3.42	FRAP
	ATOM	2029	CE1	PHE	2108	-10.170	24.461	25.396	1.00	8.79	FRAP
	ATOM	2030	CE2	PHE	2108	-9.613	22.760	27.000	1.00	9.05	FRAP
5	ATOM	2031	CZ	PHE	2108	-9.214	23.692	26.045	1.00	12.56	FRAP
	ATOM	2032	C	PHE	2108	-13.423	20.810	26.364	1.00	9.13	FRAP
	ATOM	2033	O	PHE	2108	-12.685	20.368	25.493	1.00	10.33	FRAP
	ATOM	2034	N	ARG	2109	-13.609	20.198	27.528	1.00	11.74	FRAP
	ATOM	2035	H	ARG	2109	-14.125	20.671	28.212	0.00	0.00	FRAP
10	ATOM	2036	CA	ARG	2109	-13.001	18.905	27.832	1.00	12.27	FRAP
	ATOM	2037	CB	ARG	2109	-13.358	18.476	29.256	1.00	18.36	FRAP
	ATOM	2038	CG	ARG	2109	-12.193	18.477	30.239	1.00	32.13	FRAP
	ATOM	2039	CD	ARG	2109	-11.939	17.082	30.819	1.00	43.37	FRAP
	ATOM	2040	NE	ARG	2109	-13.169	16.442	31.297	1.00	53.59	FRAP
15	ATOM	2041	HE	ARG	2109	-13.738	16.951	31.910	0.00	0.00	FRAP
	ATOM	2042	CZ	ARG	2109	-13.573	15.218	30.956	1.00	54.76	FRAP
	ATOM	2043	NH1	ARG	2109	-14.732	14.754	31.413	1.00	54.90	FRAP
	ATOM	2044	HH11	ARG	2109	-15.288	15.321	32.021	0.00	0.00	FRAP
	ATOM	2045	HH12	ARG	2109	-15.033	13.832	31.173	0.00	0.00	FRAP
20	ATOM	2046	NH2	ARG	2109	-12.812	14.444	30.188	1.00	53.94	FRAP
	ATOM	2047	HH21	ARG	2109	-11.931	14.776	29.851	0.00	0.00	FRAP
	ATOM	2048	HH22	ARG	2109	-13.130	13.529	29.944	0.00	0.00	FRAP
	ATOM	2049	C	ARG	2109	-13.454	17.829	26.849	1.00	11.58	FRAP
	ATOM	2050	O	ARG	2109	-12.682	16.939	26.509	1.00	11.33	FRAP
25	ATOM	2051	N	ARG	2110	-14.710	17.911	26.412	1.00	10.43	FRAP
	ATOM	2052	H	ARG	2110	-15.280	18.632	26.748	0.00	0.00	FRAP
	ATOM	2053	CA	ARG	2110	-15.260	16.952	25.455	1.00	10.64	FRAP
	ATOM	2054	CB	ARG	2110	-16.795	16.947	25.499	1.00	12.47	FRAP
	ATOM	2055	CG	ARG	2110	-17.418	16.320	26.743	1.00	19.35	FRAP
30	ATOM	2056	CD	ARG	2110	-17.423	14.786	26.714	1.00	31.28	FRAP
	ATOM	2057	NE	ARG	2110	-16.091	14.194	26.900	1.00	41.95	FRAP
	ATOM	2058	HE	ARG	2110	-15.389	14.432	26.260	0.00	0.00	FRAP
	ATOM	2059	CZ	ARG	2110	-15.762	13.332	27.865	1.00	41.41	FRAP
	ATOM	2060	NH1	ARG	2110	-14.534	12.815	27.899	1.00	36.39	FRAP
35	ATOM	2061	HH11	ARG	2110	-13.866	13.068	27.201	0.00	0.00	FRAP
	ATOM	2062	HH12	ARG	2110	-14.282	12.171	28.621	0.00	0.00	FRAP
	ATOM	2063	NH2	ARG	2110	-16.633	13.017	28.820	1.00	36.79	FRAP
	ATOM	2064	HH21	ARG	2110	-17.547	13.422	28.830	0.00	0.00	FRAP
	ATOM	2065	HH22	ARG	2110	-16.368	12.373	29.538	0.00	0.00	FRAP

	ATOM	2066	C	ARG	2110	-14.810	17.200	24.014	1.00	12.51	FRAP
	ATOM	2067	O	ARG	2110	-14.818	16.280	23.209	1.00	15.19	FRAP
	ATOM	2068	N	ILE	2111	-14.494	18.447	23.670	1.00	14.35	FRAP
	ATOM	2069	H	ILE	2111	-14.598	19.149	24.342	0.00	0.00	FRAP
5	ATOM	2070	CA	ILE	2111	-14.033	18.769	22.314	1.00	18.50	FRAP
	ATOM	2071	CB	ILE	2111	-14.644	20.117	21.784	1.00	14.09	FRAP
	ATOM	2072	CG2	ILE	2111	-16.148	20.108	21.982	1.00	19.97	FRAP
	ATOM	2073	CG1	ILE	2111	-14.044	21.333	22.500	1.00	13.58	FRAP
	ATOM	2074	CD1	ILE	2111	-14.821	22.615	22.301	1.00	2.00	FRAP
10	ATOM	2075	C	ILE	2111	-12.510	18.791	22.163	1.00	22.21	FRAP
	ATOM	2076	O	ILE	2111	-11.963	19.586	21.395	1.00	27.42	FRAP
	ATOM	2077	N	SER	2112	-11.840	17.887	22.870	1.00	27.11	FRAP
	ATOM	2078	H	SER	2112	-12.312	17.230	23.418	0.00	0.00	FRAP
	ATOM	2079	CA	SER	2112	-10.410	17.634	22.673	1.00	32.50	FRAP
15	ATOM	2080	CB	SER	2112	-9.590	18.179	23.852	1.00	31.61	FRAP
	ATOM	2081	OG	SER	2112	-9.589	19.601	23.899	1.00	28.34	FRAP
	ATOM	2082	HG	SER	2112	-9.617	19.750	24.846	0.00	0.00	FRAP
	ATOM	2083	C	SER	2112	-10.155	16.126	22.525	1.00	35.63	FRAP
	ATOM	2084	O	SER	2112	-10.552	15.361	23.432	1.00	36.42	FRAP
20	ATOM	2085	OT	SER	2112	-9.613	15.712	21.474	1.00	41.38	FRAP
	ATOM	2086	OH2	WATR	301	-13.963	32.282	39.005	1.00	20.07	WATR
	ATOM	2087	H1	WATR	301	-14.436	33.059	39.326	0.00	20.00	WATR
	ATOM	2088	H2	WATR	301	-13.909	31.701	39.771	0.00	20.00	WATR
	ATOM	2089	OH2	WATR	302	-0.900	21.657	34.783	1.00	23.80	WATR
25	ATOM	2090	H1	WATR	302	-1.021	21.041	35.510	0.00	20.00	WATR
	ATOM	2091	H2	WATR	302	-1.478	21.246	34.123	0.00	20.00	WATR
	ATOM	2092	OH2	WATR	303	-6.938	34.185	40.131	1.00	41.17	WATR
	ATOM	2093	H1	WATR	303	-6.199	34.542	39.638	0.00	20.00	WATR
	ATOM	2094	H2	WATR	303	-6.527	33.918	40.941	0.00	20.00	WATR
30	ATOM	2095	OH2	WATR	304	-10.919	15.222	48.819	1.00	28.06	WATR
	ATOM	2096	H1	WATR	304	-10.331	15.994	48.864	0.00	20.00	WATR
	ATOM	2097	H2	WATR	304	-10.602	14.763	48.037	0.00	20.00	WATR
	ATOM	2098	OH2	WATR	305	-21.400	35.769	26.707	1.00	26.77	WATR
	ATOM	2099	H1	WATR	305	-21.139	35.329	27.513	0.00	20.00	WATR
35	ATOM	2100	H2	WATR	305	-22.356	35.778	26.710	0.00	20.00	WATR
	ATOM	2101	OH2	WATR	306	0.813	27.087	37.460	1.00	15.38	WATR
	ATOM	2102	H1	WATR	306	0.278	27.451	36.742	0.00	20.00	WATR
	ATOM	2103	H2	WATR	306	0.156	26.516	37.895	0.00	20.00	WATR
	ATOM	2104	OH2	WATR	307	-30.428	31.660	28.013	1.00	46.41	WATR

	ATOM	2105	H1	WATR	307	-30.299	30.737	27.805	0.00	20.00	WATR
	ATOM	2106	H2	WATR	307	-30.248	31.722	28.946	0.00	20.00	WATR
	ATOM	2107	OH2	WATR	308	-4.519	32.837	47.558	1.00	15.92	WATR
	ATOM	2108	H1	WATR	308	-4.435	32.964	48.515	0.00	20.00	WATR
	ATOM	2109	H2	WATR	308	-4.287	31.920	47.465	0.00	20.00	WATR
	ATOM	2110	OH2	WATR	309	-18.089	22.614	12.803	1.00	25.97	WATR
	ATOM	2111	H1	WATR	309	-17.511	23.005	12.138	0.00	20.00	WATR
	ATOM	2112	H2	WATR	309	-18.955	22.733	12.394	0.00	20.00	WATR
	ATOM	2113	OH2	WATR	310	-22.152	21.619	36.180	1.00	41.59	WATR
	ATOM	2114	H1	WATR	310	-22.437	22.341	36.738	0.00	20.00	WATR
	ATOM	2115	H2	WATR	310	-22.872	21.464	35.569	0.00	20.00	WATR
	ATOM	2116	OH2	WATR	311	-6.459	3.543	52.877	1.00	32.94	WATR
	ATOM	2117	H1	WATR	311	-6.280	2.752	52.368	0.00	20.00	WATR
	ATOM	2118	H2	WATR	311	-5.832	4.191	52.543	0.00	20.00	WATR
	ATOM	2119	OH2	WATR	312	-5.993	11.471	28.804	1.00	18.59	WATR
	ATOM	2120	H1	WATR	312	-6.909	11.725	28.881	0.00	20.00	WATR
	ATOM	2121	H2	WATR	312	-5.782	11.031	29.653	0.00	20.00	WATR
	ATOM	2122	OH2	WATR	313	-0.619	20.784	55.049	1.00	19.50	WATR
	ATOM	2123	H1	WATR	313	-0.854	20.074	55.637	0.00	20.00	WATR
	ATOM	2124	H2	WATR	313	-1.113	21.551	55.388	0.00	20.00	WATR
	ATOM	2125	OH2	WATR	314	-5.598	26.321	58.876	1.00	36.20	WATR
	ATOM	2126	H1	WATR	314	-6.497	26.108	58.602	0.00	20.00	WATR
	ATOM	2127	H2	WATR	314	-5.118	25.491	58.861	0.00	20.00	WATR
	ATOM	2128	OH2	WATR	315	-3.023	33.604	37.769	1.00	26.43	WATR
	ATOM	2129	H1	WATR	315	-2.394	34.283	37.516	0.00	20.00	WATR
	ATOM	2130	H2	WATR	315	-3.855	33.984	37.469	0.00	20.00	WATR
	ATOM	2131	OH2	WATR	316	-25.006	29.561	22.950	1.00	41.75	WATR
	ATOM	2132	H1	WATR	316	-24.532	29.047	23.605	0.00	20.00	WATR
	ATOM	2133	H2	WATR	316	-25.677	28.934	22.652	0.00	20.00	WATR
	ATOM	2134	OH2	WATR	317	-23.638	29.893	10.609	1.00	16.55	WATR
	ATOM	2135	H1	WATR	317	-23.016	29.169	10.621	0.00	20.00	WATR
	ATOM	2136	H2	WATR	317	-24.395	29.529	11.101	0.00	20.00	WATR
	ATOM	2137	OH2	WATR	318	-7.744	6.880	50.272	1.00	20.83	WATR
	ATOM	2138	H1	WATR	318	-7.080	6.901	49.564	0.00	20.00	WATR
	ATOM	2139	H2	WATR	318	-7.480	6.116	50.785	0.00	20.00	WATR
	ATOM	2140	OH2	WATR	319	-2.748	2.703	46.777	1.00	31.05	WATR
	ATOM	2141	H1	WATR	319	-3.202	3.462	46.395	0.00	20.00	WATR
	ATOM	2142	H2	WATR	319	-3.353	2.352	47.432	0.00	20.00	WATR
	ATOM	2143	OH2	WATR	320	-19.295	42.654	40.303	1.00	39.42	WATR

ATOM	2144	H1	WATR	320	-19.042	41.825	39.876	0.00	20.00	WATR
ATOM	2145	H2	WATR	320	-18.638	43.269	39.991	0.00	20.00	WATR
ATOM	2146	OH2	WATR	321	0.583	32.369	55.901	1.00	39.29	WATR
ATOM	2147	H1	WATR	321	-0.191	32.008	55.428	0.00	20.00	WATR
ATOM	2148	H2	WATR	321	1.272	31.719	55.776	0.00	20.00	WATR
ATOM	2149	OH2	WATR	322	-16.781	17.874	51.246	1.00	33.48	WATR
ATOM	2150	H1	WATR	322	-17.172	18.545	50.688	0.00	20.00	WATR
ATOM	2151	H2	WATR	322	-15.838	18.064	51.228	0.00	20.00	WATR
ATOM	2152	OH2	WATR	323	-19.829	12.916	46.549	1.00	26.46	WATR
ATOM	2153	H1	WATR	323	-19.808	13.873	46.697	0.00	20.00	WATR
ATOM	2154	H2	WATR	323	-19.224	12.538	47.193	0.00	20.00	WATR

Note: FKBP sequence is SEQ ID NO: 1

FRAP sequence is SEQ ID NO: 2

SEQUENCE LISTING

(1) GENERAL INFORMATION:

(i) APPLICANT: CORNELL RESEARCH FOUNDATION, INC.

(ii) TITLE OF INVENTION: CRYSTALLINE FRAP COMPLEX

(iii) NUMBER OF SEQUENCES: 2

(iv) CORRESPONDENCE ADDRESS:
(A) ADDRESSEE: ARIAD Pharmaceuticals, Inc.
(B) STREET: 26 Landsdowne Street
(C) CITY: Cambridge
(D) STATE: MA
(E) COUNTRY: USA
(F) ZIP: 02139-4234

(v) COMPUTER READABLE FORM:
(A) MEDIUM TYPE: Floppy disk
(B) COMPUTER: IBM PC compatible
(C) OPERATING SYSTEM: PC-DOS/MS-DOS
(D) SOFTWARE: PatentIn Release #1.0, Version #1.30

(vi) CURRENT APPLICATION DATA:
(A) APPLICATION NUMBER:
(B) FILING DATE: HEREWITH
(C) CLASSIFICATION:

(vii) PRIOR APPLICATION DATA:
(A) APPLICATION NUMBER: US 60/005,808
(B) FILING DATE: 23-OCT-1995

(vii) PRIOR APPLICATION DATA:
(A) APPLICATION NUMBER: US 60/006,069
(B) FILING DATE: 24-OCT-1995

(viii) ATTORNEY/AGENT INFORMATION:

(A) NAME: BERSTEIN, David L.

(B) REGISTRATION NUMBER: 31,235

(C) REFERENCE/DOCKET NUMBER: ARIAD 350A-PCT

(ix) TELECOMMUNICATION INFORMATION:

(A) TELEPHONE: 617-494-0400

(B) TELEFAX: 617-494-0208

(2) INFORMATION FOR SEQ ID NO:1:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 107 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:1:

```
Gly Val Gln Val Glu Thr Ile Ser Pro Gly Asp Gly Arg Thr Phe Pro
1               5                  10                  15

Lys Arg Gly Gln Thr Cys Val Val His Tyr Thr Gly Met Leu Glu Asp
            20                  25                  30

Gly Lys Lys Phe Asp Ser Ser Arg Asp Arg Asn Lys Pro Phe Lys Phe
        35                  40                  45

Met Leu Gly Lys Gln Glu Val Ile Arg Gly Trp Glu Glu Gly Val Ala
    50                  55                  60

Gln Met Ser Val Gly Gln Arg Ala Lys Leu Thr Ile Ser Pro Asp Tyr
65                  70                  75                  80

Ala Tyr Gly Ala Thr Gly His Pro Gly Ile Ile Pro Pro His Ala Thr
                85                  90                  95
```

Leu Val Phe Asp Val Glu Leu Leu Lys Leu Glu
100 105

(2) INFORMATION FOR SEQ ID NO:2:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 100 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:2:

Glu Leu Ile Arg Val Ala Ile Leu Trp His Glu Met Trp His Glu Gly
1 5 10 15

Leu Glu Glu Ala Ser Arg Leu Tyr Phe Gly Glu Arg Asn Val Lys Gly
20 25 30

Met Phe Glu Val Leu Glu Pro Leu His Ala Met Met Glu Arg Gly Pro
35 40 45

Gln Thr Leu Lys Glu Thr Ser Phe Asn Gln Ala Tyr Gly Arg Asp Leu
50 55 60

Met Glu Ala Gln Glu Trp Cys Arg Lys Tyr Met Lys Ser Gly Asn Val
65 70 75 80

Lys Asp Leu Thr Gln Ala Trp Asp Leu Tyr Tyr His Val Phe Arg Arg
85 90 95

Ile Ser Lys Gln
100

Claims

1. A crystalline composition comprising a complex formed by a first protein containing an FRB domain, a second protein containing an FKBP domain and a ligand capable of forming a ternary complex with the first and second proteins.

2. A composition of claim 1 in which the complex is characterized by the coordinates of Appendix I, or by coordinates having a root mean square deviation therefrom, with respect to conserved backbone atoms of the listed amino acids, of not more than 1.5 Å.

3. A machine-readable data storage medium, comprising a data storage material encoded with machine readable data which, when using a machine programmed with instructions for using said data, is capable of displaying a graphical three-dimensional representation of a molecule or molecular complex comprising a protein containing an FRB domain.

4. A machine-readable data storage medium of claim 3 in which the machine readable data includes data corresponding to the coordinates for the FRB domain set forth in Appendix I, or coordinates having a root mean square deviation therefrom, with respect to conserved protein backbone atoms, of not more than 1.5 Å.

5. A machine-readable data storage medium comprising a data storage material encoded with a first set of machine readable data which, when combined with a second set of machine-readable data, using a machine programmed with instructions for using said first set of data and said second set of data, can determine at least a portion of the coordinates corresponding to the second set of machine-readable data, wherein: said first set of data comprises a Fourier transform of at least a portion of the coordinates of the FRB domain set forth in Appendix I and said second set of data comprises an X-ray diffraction pattern of a molecule or molecular complex.

6. A method for displaying a three dimensional representation of a composition of claims 1 or 2 which comprises:

(a) providing a machine capable of reading data stored on a machine-readable storage medium of any of claims 3-5, programmed with instructions for using said data to display a graphical three-dimensional representation of a protein or protein:ligand complex or portion thereof defined by said data, and loaded with a machine-readable storage medium of any of claims 3-5; and,

(b) permitting the machine to read said data and display the three-dimensional representation.

7. A method for determining the three-dimensional structure of a protein containing an FRB domain, or a complex of such protein with a ligand therefor, which comprises

(a) obtaining x-ray diffraction data for crystals of the protein or complex,

(b) providing three-dimensional structural coordinates for a composition of claims 1 or 2, and

(c) determining the three-dimensional structure of the protein or complex by analyzing the x-ray diffraction data with reference to the previous structural coordinates using molecular replacement techniques.

8. A method for determining the three dimensional structure of a protein containing an an FRB domain or co-complex of said protein with a ligand therefor, which method comprises:

(a) providing structural coordinates for a composition of claims 1 or 2, and

(b) determining the three-dimensional structure of the FRB domain-containing protein or complex by homology modeling with reference to the previous structural coordinates.

9. A method for selecting a compound capable of binding to an FRB domain which comprises:

(a) providing coordinates defining the three dimensional structure of the FRB domain;

(b) characterizing points associated with that three dimensional structure with respect to the favorability of interactions with one or more selected functional groups;

(c) providing a database of one or more candidate compounds; and

(d) identifying from the database those compounds having structures which best fit the points of favorable interaction with the three dimensional structure.

10. A method of claim 9 which further comprises testing a compound so identified for its ability to:

(a) bind to FRAP, with or without FKBP12,

(b) inhibit the binding of rapamycin or FKBP12:rapamycin to FRAP, and/or

(c) trigger a biological function mediated by rapamycin.

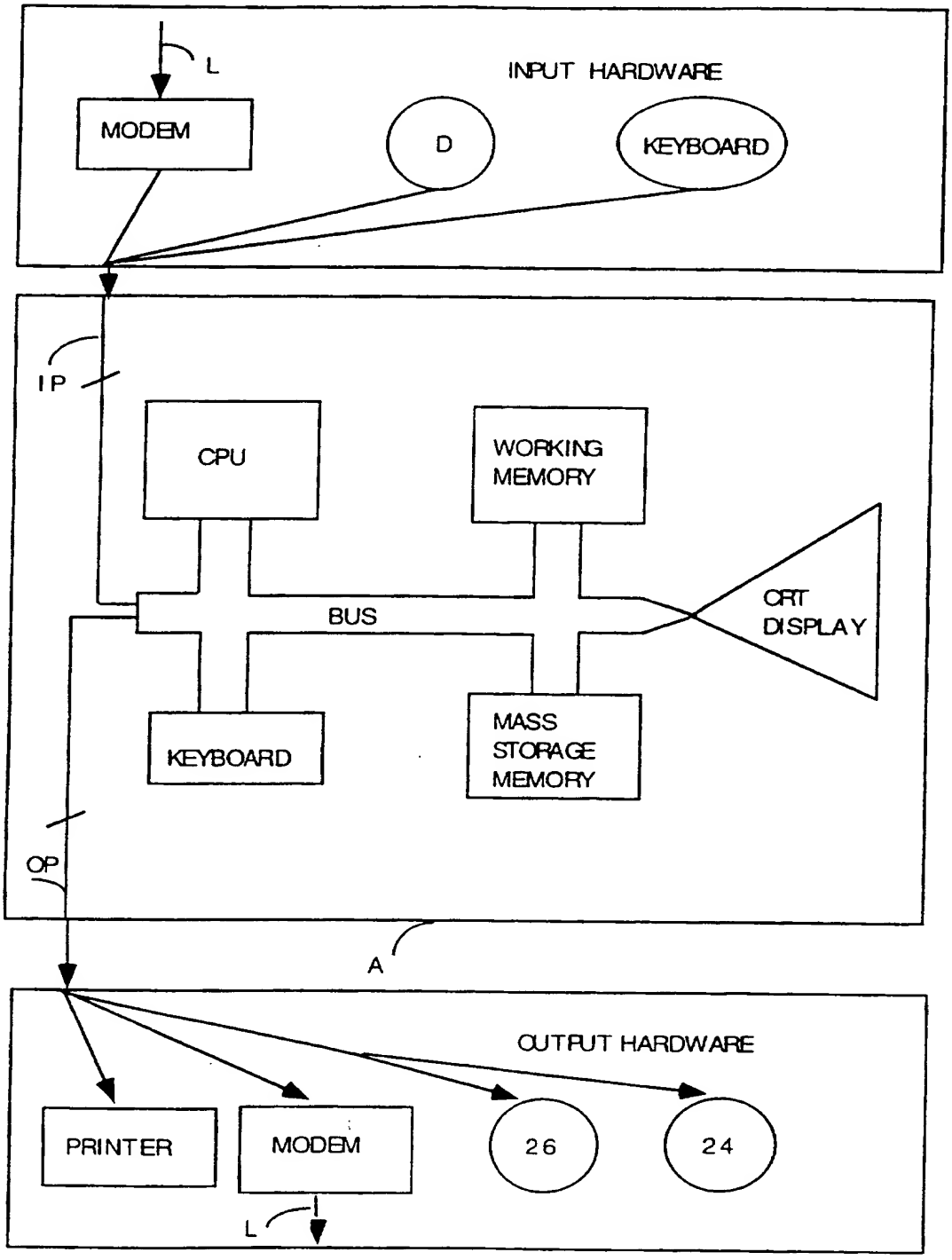

FIG. 1

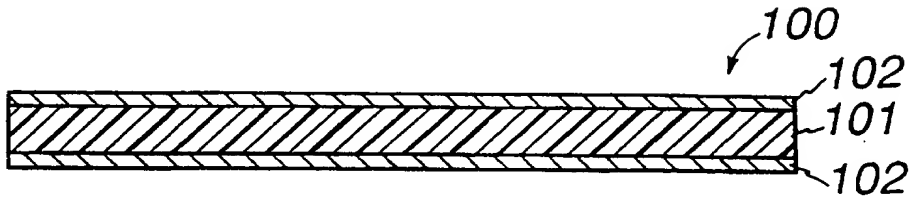

Fig. 2A

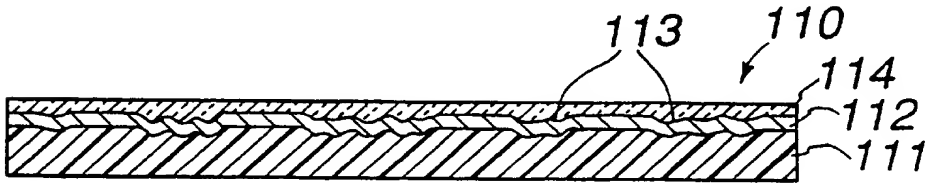

Fig. 2B

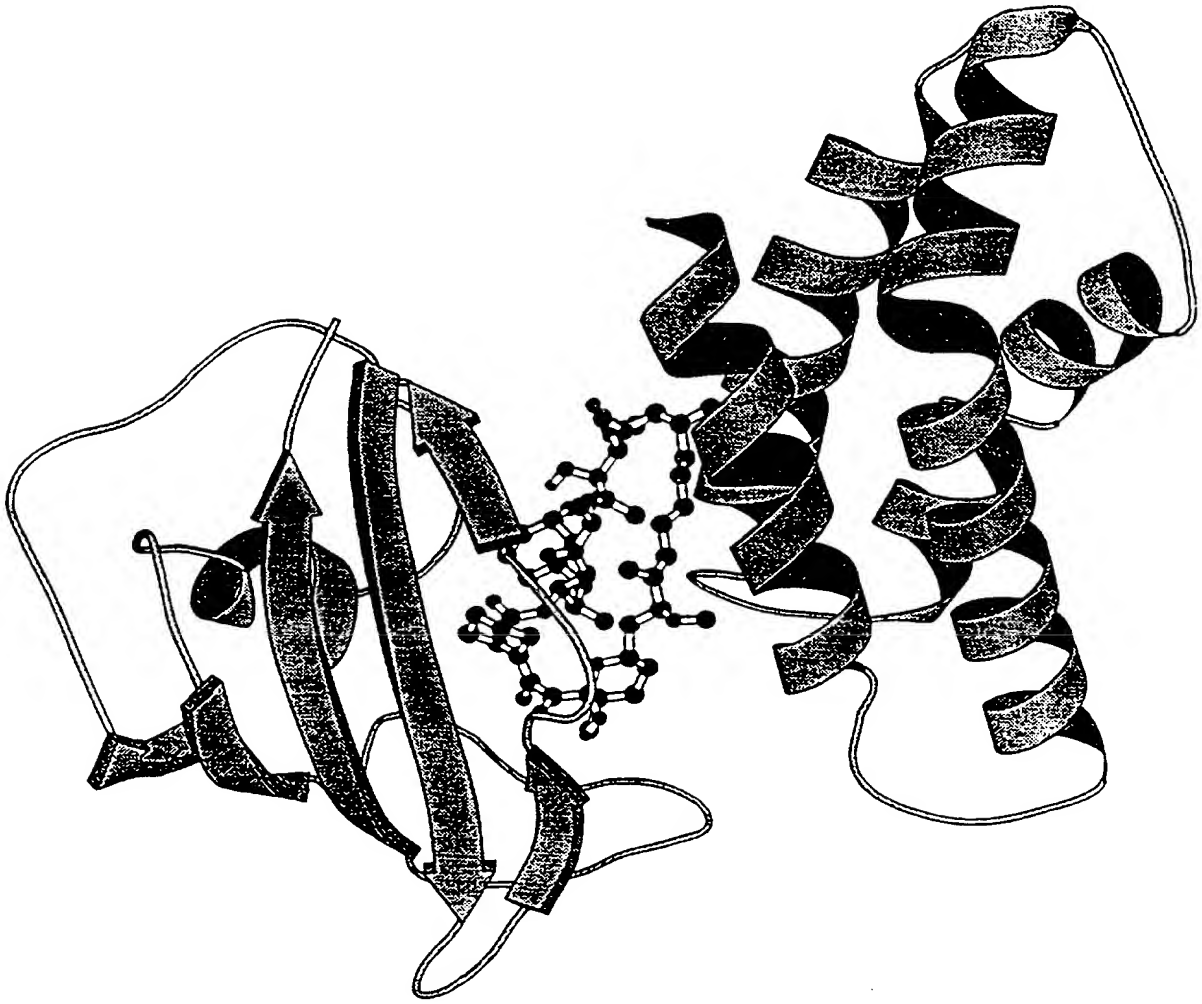

FIG. 3

INTERNATIONAL SEARCH REPORT

International Application No
PCT/US 96/16953

A. CLASSIFICATION OF SUBJECT MATTER
IPC 6 C12N9/12 G06F17/50

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 6 C12N G06F

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF USA, vol. 92, May 1995, WASHINGTON US, pages 4947-4951, XP002023699 J CHEN E.A.: "Identification of an 11 kDa FKBP12-rapamycin binding domain within the 289 kDa FRAP..." cited in the application see the whole document ---	1-10
Y	NATURE, vol. 369, 30 June 1994, LONDON GB, pages 756-758, XP002023700 E.J.BROWN E.A.: "A mammalian protien targeted by G1-arresting rapamycin-receptor complex" cited in the application see the whole document ---	1-10

-/--

[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
29 January 1997	03. 02. 97

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+ 31-70) 340-2040, Tx. 31 651 epo nl, Fax (+ 31-70) 340-3016	Groenendijk, M

Form PCT/ISA/210 (second sheet) (July 1992)

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	J.MOL.BIOL., vol. 229, no. 1, 1993, page 105-124 XP000616336 G.D. VAN DUYNE E.A.: "Atomic structures of the human immunophilin FKBP12 complexes with FK506 and rapamycin" cited in the application See especially page 107, column 2 under b	1-10
Y	CELL, vol. 82, 11 August 1995, NA US, pages 507-522, XP002023702 J.P.GRIFFITH E.A.: "X-ray structure of calcineurin inhibited by the immunophilin-immunosuppressant FKBP12-FK506 complex" cited in the application See especially page 519	1-10
Y	WO 94 25860 A (IMMUNEX CORP) 10 November 1994 see the whole document	2-10
Y	US 5 353 236 A (SUBBIAH SUBRAMANIAN) 4 October 1994 see the whole document	2-10
Y	EP 0 676 471 A (AMERICAN HOME PROD ;UNIV COLUMBIA (US)) 11 October 1995 The whole document; see especially page 5, line 39 to page 6, line 8; claims 21,23,25	9,10
P,X	SCIENCE, vol. 273, 12 July 1996, LANCASTER, PA US, pages 239-242, XP002023703 J CHOI E.A.: "Structure of FKBP12-rapamycin complex interacting with the binding domain of human FRAP" see the whole document	1-10

INTERNATIONAL SEARCH REPORT

[redacted]ational application No.
PCT/US 96/ 16953

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. [X] Claims Nos.: 3-6
because they relate to subject matter not required to be searched by this Authority, namely:

Remark: Although these claims are directed to a representation of information on a carrier and a process for presenting this information, the search has been carried out as far as possible and based on the molecular structure represented by this information (Art.17/R.39.1)

2. [ ] Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

3. [ ] Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. [ ] As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. [ ] As all searchable claims could be searches without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. [ ] As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. [ ] No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

[ ] The additional search fees were accompanied by the applicant's protest.

[ ] No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

Information on patent family members

Inter ial Application No
PCT/US 96/16953

Patent document cited in search report	Publication date	Patent family member(s)		Publication date
WO-A-9425860	10-11-94	US-A-	5453937	26-09-95
		AU-A-	6779994	21-11-94
		US-A-	5557535	17-09-96
US-A-5353236	04-10-94	WO-A-	9322740	11-11-93
EP-A-0676471	11-10-95	AU-A-	1367095	14-09-95
		CA-A-	2144223	09-09-95
		HU-A-	72189	28-03-96
		JP-A-	8059696	05-03-96